# U.S. Army Center for Health Promotion and Preventive Medicine

EPIDEMIOLOGIC CONSULTATION NO. 29-HE-8091b-98
Investigation of an Outbreak of Rapidly-Growing Mycobacteria (RGM) among Bone-Marrow Transplant (BMT) Unit Patients
Brooke Army Medical Center (BAMC)
Fort Sam Houston, Texas
June 1998

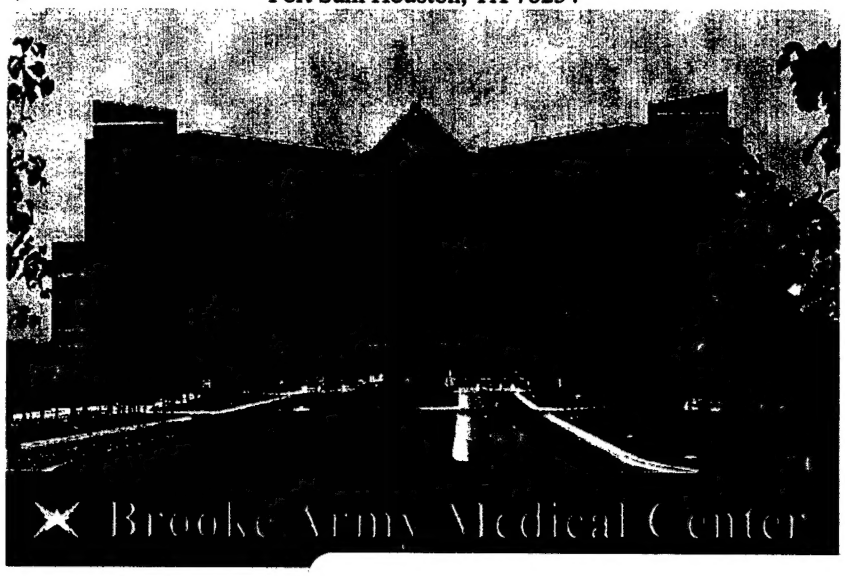
COL Jose L. Sanchez, LTC Roberto N. Nang, Dr. (COL Ret) John F. Brundage, Jerry A. Valcik, Jennifer L. Filippelli, John K. Brokaw

U.S. Army Center for Health Promotion & Preventive Medicine
Directorate of Epidemiology & Disease Surveillance
Directorate of Clinical Preventive Medicine
Directorate of Environmental Health Engineering
5158 Blackhawk Road
Aberdeen Proving Ground, MD 21010-5403

and

MAJ Robert M. Plemmons, LTC Susan L. Fraser, COL David P. Dooley
LTC Dana Gruber, MAJ Bethany A. Alexander, MAJ Rickey C. Myhand,
LTC Kenneth J. Tannen

Brooke Army Medical Center
3851 Roger Brooke Drive
Fort Sam Houston, TX 78234






USCHPPM

Readiness Thru Health

## *U.S. Army Center for Health Promotion and Preventive Medicine*

*The lineage of the U.S. Army Center for Health Promotion and Preventive Medicine (USACHPPM) can be traced back over 50 years. This organization began as the U.S. Army Industrial Hygiene Laboratory, established during the industrial buildup for World War II, under the direct supervision of the Army Surgeon General. Its original location was at the Johns Hopkins School of Hygiene and Public Health. Its mission was to conduct occupational health surveys and investigations within the Department of Defense's (DOD's) industrial production base. It was staffed with three personnel and had a limited annual operating budget of three thousand dollars.*

*Most recently, it became internationally known as the U.S. Army Environmental Hygiene Agency (AEHA). Its mission expanded to support worldwide preventive medicine programs of the Army, DOD, and other Federal agencies as directed by the Army Medical Command or the Office of The Surgeon General, through consultations, support services, investigations, on-site visits, and training.*

*On 1 August 1994, AEHA was redesignated the U.S. Army Center for Health Promotion and Preventive Medicine with a provisional status and a commanding general officer. On 1 October 1995, the nonprovisional status was approved with a mission of providing preventive medicine and health promotion leadership, direction, and services for America's Army.*

*The organization's quest has always been one of excellence and the provision of quality service. Today, its goal is to be an established world-class center of excellence for achieving and maintaining a fit, healthy, and ready force. To achieve that end, the CHPPM holds firmly to its values which are steeped in rich military heritage:*

★ *Integrity is the foundation*
★ *Excellence is the standard*
★ *Customer satisfaction is the focus*
★ *Its people are the most valued resource*
★ *Continuous quality improvement is the pathway*

*This organization stands on the threshold of even greater challenges and responsibilities. It has been reorganized and reengineered to support the Army of the future. The CHPPM now has three direct support activities located in Fort Meade, Maryland; Fort McPherson, Georgia; and Fitzsimons Army Medical Center, Aurora, Colorado; to provide responsive regional health promotion and preventive medicine support across the U.S. There are also two CHPPM overseas commands in Landstuhl, Germany and Camp Zama, Japan who contribute to the success of CHPPM's increasing global mission. As CHPPM moves into the 21st Century, new programs relating to fitness, health promotion, wellness, and disease surveillance are being added. As always, CHPPM stands firm in its commitment to Army readiness. It is an organization proud of its fine history, yet equally excited about its challenging future.*

# REPORT DOCUMENTATION PAGE

*Form Approved*
*OMB No. 0704-0188*



| 1. AGENCY USE ONLY *(Leave blank)* | 2. REPORT DATE | 3. REPORT TYPE AND DATES COVERED |
|---|---|---|
| | November 1999 | Final |

**4. TITLE AND SUBTITLE**
Investigation of an Outbreak of Rapidly-Growing Mycobacteria (RGM) among Bone-Marrow Transplant (BMT) Unit Patients Brooke Army Medical Center (BAMC) Fort Sam Houston, Texas June 1998

**5. FUNDING NUMBERS**

**6. AUTHOR(S)**
COL Jose Sanchez, LTC Roberto Nang, Dr.John Brundage, Jerry Valcik, Jennifer Filippelli, John Brokaw, MAJ Robert Plemmons, Ltc Susan Fraser, COL David Dooley, LTC Dana Gruber, MAJ Bethany Alexander, MAJ Rickey Myhand

**7. PERFORMING ORGANIZATION NAME(S) AND ADDRESS(ES)**
U.S. Army Center for Health Promotion & Preventive Medicine, Directorate of Epidemiology & Disease Surveillance, Directorate of Clinical Preventive Medicine, Directorate of Environmental Health Engineering 5158 Blackhawk Road Aberdeen Proving Ground, MD 21010-5403 and Brooke Army Medical Center 3851 Roger Brooke Drive Fort Sam Houston, TX 78234

**8. PERFORMING ORGANIZATION REPORT NUMBER**
29-HE-8091b-98

**9. SPONSORING / MONITORING AGENCY NAME(S) AND ADDRESS(ES)**
U.S. Army Center for Health Promotion & Preventive Medicine, Directorate of Epidemiology & Disease Surveillance, Directorate of Clinical Preventive Medicine, Directorate of Environmental Health Engineering 5158 Blackhawk Road Aberdeen Proving Ground, MD 21010-5403 and Brooke Army Medical Center 3851 Roger Brooke Drive Fort Sam Houston, TX 78234

**10. SPONSORING / MONITORING AGENCY REPORT NUMBER**

**11. SUPPLEMENTARY NOTES**

**12a. DISTRIBUTION / AVAILABILITY STATEMENT**

Approved for Public Release, Distribution is Unlimited

**12b. DISTRIBUTION CODE**

**13. ABSTRACT** *(Maximum 200 words)*

An epidemiologic consultation (EPICON) investigation was conducted during the month of June 1998 to examine reports of increased number of rapidly-growing mycobacteria (RGM) among bone marrow transplant (BMT) patients at Brooke Army Medical Center, San Antonio, Texas. Upon request, a team from the USACHPPM assisted the BAMC staff to identify and characterize risk factors for RGM infection and to develop intervention control plans.

The initial review of cases revealed a high rate of RGM infection (10 cases in 75 patients, rate of 13.3%) in BMT unit patients during FY98 (Oct 97-May 98). A case-control study was undertaken involving all 14 cases and two control groups, an "internal" group (non-infected patients at the BMT unit, n=23) and an "external" group (non-infected patients at the Heme-onc ward, n=23). Only central venous (CV) catheter inflammation (AOR=7.63, 95% CI 1.32-44.08) and a positive blood culture (AOR=6.38, 95% CI 1.06-38.39) during hospitalization were correlated with RGM infection risk.

Mycobacterial culture and pulse-field gel electrophoresis (PFGE) DNA typing revealed several patient isolates similar to water sample isolates recovered simultaneously from the BAMC potable water system. Recommendations for control of contamination of the BAMC water system were made and efforts to control this problem are ongoing.

**14. SUBJECT TERMS**
Rapidly-growing mycobacteria, Catheter, Water Treatment Plants

**15. NUMBER OF PAGES**
59

**16. PRICE CODE**

| 17. SECURITY CLASSIFICATION OF REPORT | 18. SECURITY CLASSIFICATION OF THIS PAGE | 19. SECURITY CLASSIFICATION OF ABSTRACT | 20. LIMITATION OF ABSTRACT |
|---|---|---|---|
| Unclassified | Unclassified | Unclassified | |

## TABLE of CONTENTS

Epidemiologic Consultation No. 29-HE-8091b-98
Investigation of an Outbreak of Rapidly-Growing Mycobacteria (RGM)
among Bone-Marrow Transplant (BMT) Unit Patients
Brooke Army Medical Center (BAMC)
Fort Sam Houston, Texas
June 1998

## EXECUTIVE SUMMARY

During the period of 1 April 1997 through early June 1998 a total of 14 cases of infection with rapidly-growing mycobacteria (RGM) was detected by infection control personnel among inpatients at Brooke Army Medical Center (BAMC). Initial laboratory identification at BAMC mycobacteria section reported that five (36%) of these patients sustained *M. chelonae* infections, 5 (36%) had *M. fortuitum*, 2 (14%) had *M. abscessus* and 2 (14%) had mixed types (*both M. chelonae & M. fortuitum* species). Thirteen of these 14 cases had received autologous peripheral blood stem cell infusions at the bone marrow transplantation (BMT) unit; the remaining patient had been admitted to the Hematology-oncology (Heme-onc) ward for a myelodysplastic syndrome. Upon request, a team from the USACHPPM assisted the BAMC staff to identify and characterize risk factors for RGM infection and to develop necessary intervention control plans.

Upon initial review of cases, the RGM rate of infection in BMT unit patients during FY98 (Oct 97-May 98) was found to be very high (10 cases in 75 patients, rate of 13.3 per 100). By comparison, the infection rate in FY97 was onlyof only 3.3% (3 of 90 patients) in FY97 (Oct 96-Sep 97) and no (0 of 158 patients) infections detected during the period of Oct 92 – Sep 96 (FY93-FY96. By comparison, the BMT program at a large reference center (University of Minnesota Hospital) reported only seven RGM infections among 2,241 BMT recipients over a 20-year period (rate of 0.3 per 100 BMTs) and two other non-military hospitals reported no cases among 772 BMT patients during the same period. Thus, BAMC's recent BMT-related RGM experience markedly varied from its own prior and from others' reported experiences.

To assess hospital-acquired infection experience on the BMT unit, RGM and staphylococcal (*S. aureus, S. epidermidis*) infection rates were compared between BMT unit patients and a comparable group of immunosuppressed patients in the hematology-oncology (Heme-onc) ward who had not received bone marrow transplants. RGM infection rates (per 1,000 patient-days) were found to be nearly 30 times higher (3.26 per 1,000 patient-days) for BMT unit patients as compared to only a rate of 0.12 per 1,000 patient-days for Heme-onc patients. Staphylococcal infection rates, however, were only slightly higher among Heme-onc than BMT unit patients (BMT rate of 1.26 per 1,000 patient-days compared to a Heme-onc rate of 2.32 per 1,000 patient-days). In addition, no breakdown in infection control procedures were detected at the BMT unit. Thus, the increased rate of RGM infections among BMT unit patients did not seem to reflect a predisposing breakdown of infection control diligence.

To identify and quantify specific correlates of infection risk, a case-control study was undertaken involving all 14 cases and two referent or control groups, an "internal" one (non-infected patients at the BMT unit, n=23) and an "external" one (non-infected patients at the Heme-onc ward, n=23). Cases were compared to noncases with relation to demographic, medical, and procedure-related characteristics. Noncases were selected at random from among patients admitted in the same month as cases. Among BMT patients, RGM cases were slightly older, more often Caucasian, more likely to have intercurrent chronic illnesses, less likely to smoke, and have a higher mean maximum temperature than noncases. Also, 85% of BMT cases developed positive blood cultures during hospitalization compared to only 31% of noncases ($P < 0.05$). More BMT unit cases than noncases were also seen to develop signs of central venous (CV) catheter inflammation (at the insertion site and/or the subcutaneous tunnel) although the difference was not statistically significant. Among BMT cases and Heme-onc controls, cases were more likely to be female, have a history of breast cancer, have evidence of mucositis (inflammation and erosion of mucosal surfaces) during hospitalization, and have signs of CV catheter inflammation. On multivariate analysis that included cases and both internal and external controls (adjusted for effects of age, gender and race) only central venous (CV) catheter inflammation (AOR=7.63, 95% CI 1.32-44.08) and a positive blood culture (AOR=6.38, 95% CI 1.06-38.39) during hospitalization were statistically significantly correlated with RGM infection risk. There were no associations found between RGM infection risk and either type of, manufacturer of, or the physician who inserted the CV catheters of BMT unit patients.

The BAMC potable water supply is provided by the Fort Sam Houston (FSH) water treatment plant. Before centrally treated water is distributed within the hospital, however, it is retreated to adjust its "softness" and its chlorine content. Repeated sampling performed on March through May 1998 found an increased number of samples positive for mycobacteria. Sample from throughout the hospital, at the point of entry to BAMC, and from BAMC's water softener units (including resin, effluent and backwash) were positive for RGM. In contrast, untreated water from the aquifer that serves FSH (and much of central Texas) and finished water from the main post plant were negative for mycobacteria. Concomitant water mycobacterial culture and pulse-field gel electrophoresis (PFGE) DNA typing revealed that several patient isolates were similar to water sample isolates recovered at the same time from the BAMC potable water system. Thus, it appeared that the water from the main post treatment plant was becoming contaminated in the pipeline between the main post and the hospital (or possibly at its point of entry into the hospital). It is also very likely that the BAMC's system of three water softeners served as an amplifying mechanism for maintenance of RGMs within the hospital's potable water system.

A large number of recommendations for control of contamination of the BAMC water system were made to control this problem to include a multi-phase water system clean-up involving hot water flushing and hyperchlorination. Follow-up cultures of BAMC's water system after initial hot water flushing of BMT unit and Heme-onc ward areas in June 1998 and hospital-wide hyperchlorination in November 1998 showed no RGMs. However, subsequent samples collected in April 1999 from same sources (including the BMT unit) showed heavy growth of RGMs. Subsequent installation of water filters and/or ultraviolet (UV) lights for the water system at the BMT unit and the Heme-onc ward are being presently implemented by BAMC engineering authorities.

Epidemiologic Consultation No. 29-HE-8091b-98
Investigation of an Outbreak of Rapidly-Growing Mycobacteria (RGM)
among Bone-Marrow Transplant (BMT) Unit Patients
Brooke Army Medical Center (BAMC)
Fort Sam Houston, Texas
June 1998

## INTRODUCTION

This epidemiologic consultation was initiated in response to a concern by the Chairman, BAMC Infection Control Committee, MAJ Robert Plemmons, and the Chief, Infectious Disease Service, COL David Dooley in late May 1998. An original communication was established with Dr. John Brundage, Epidemiologist, Army Medical Surveillance Activity (AMSA), Directorate of Epidemiology and Disease Surveillance (DEDS) on 22 May. In this phone consultation COL Dooley outlined the need to investigate a cluster of 13 bone marrow transplant (BMT) patients suffering from rapidly-growing mycobacterial (RGM) infections during the period of May 1997 through May 1998. Specifically, these group of patients underwent BMT procedures at BAMC and subsequently developed bacteremia and/or central venous (CV) catheter site infection with *Mycobacterium fortuitum* or *M. chelonae*.

In order to detect possible association(s) between the in-hospital water consumption and/or exposure and the perceived relative increase in numbers of BMT patients with RGM infections, mycobacterial culture analyses were undertaken of the BAMC's potable water system starting in February 1998. Initial cultures positive for *Mycobacteria spp.* were detected as early as March 1998 (see Results section below for details). Given this information, additional experts from the Water Supply Management (Program 31), Directorate of Environmental Health Engineering (DEHE), were consulted and tasked to provide appropriate recommendations to mitigate RGM water contamination risk.

## TASKING for EPICON

On 4 June 1998, BG Harold Timboe, Commander, BAMC, and BG Patrick Sculley, Commander, USACHPPM agreed telephonically to the need for an EPICON tasking. Telephonic coordination was established between COL Dooley and COL Jose L. Sanchez, Manager, Epidemiology Services (Program 29) and an EPICON team of six USACHPPM personnel was assembled and traveled to BAMC during the period of 8-13 June 1998. This team was comprised of three medical epidemiologists, COL Sanchez (EPICON team chief), Dr. Brundage, and MAJ Roberto N. Nang; as well as three Water Supply Management Program, DEHE specialists, Mr. Jerry A. Valcik, Mr. John K. Brokaw, and Ms. Jennifer L. Filippelli.

## BACKGROUND MEDICAL INFORMATION

Bone marrow transplantation with intravenous infusion of bone marrow stem cells was first attempted in humans in 1939. As knowledge developed regarding the supportive and immunosuppressive treatments necessary, such procedures became part of established clinical therapy for the treatment of unretractable lymphoma, leukemia, solid tumors (especially breast cancer), aplastic anemia, immunodeficiency syndromes, thalassemia, and genetic-metabolic disorders (1). There are now approximately 15,000 allogeneic and autologous BMTs performed worldwide (2).

Bone marrow transplant (BMT) recipients have depleted cell-mediated immune (CMI) systems due to their underlying disease(s), pre-transplant chemotherapy and radiotherapy, graft-versus-host-disease (GVHD), transplant-related procedures, and/or complications from the above-named treatments. A high incidence of mycobacterial and other infections might be expected in these patients (1). A recently published 20-year review of experience at the BMT program, University of Minnesota Hospital, a large non-military transplant center, documented only 7 RGM infections among 2241 BMT recipients for an overall incidence of 0.3% (3). In this, the largest published-to-date review, 5 of the 7 RGM infections were sustained at the site of the CV catheter and one patient developed a vertebral disc space ($T_9$-$T_{10}$) body infection. Moreover, only one of 755 (0.1%) autologous BMT recipients developed an RGM infection.

Two other published reports of mycobacterial infections in BMT patients, published in the early 1980s have reported similarly low incidence of such infections (4,5). Navari *et al* (4) reported seven mycobacterial infections (none of which was due to RGM) among a series of 682 patients with leukemia who received allogeneic bone marrow grafts. In a second review, Kurzrock *et al* (5) reported only three mycobacterial pulmonary infections (none due to RGMs) in a series of 90 BMT patients with leukemias or aplastic anemia. In comparison to the above-named 3 studies, the occurrence of 13 RGM cases among approximately 100 BMT patients at BAMC (annual incidence = 13%) significantly exceeds the expected "normal" baseline rate for these infections.

Like all mycobacteria, RGMs possess a lipid-rich, water-repellent coat, which allows them to persist in aquatic environments, including chlorinated water supplies and piped water systems (6). Their high degree of cell wall hydrophobicity also accounts for their marked adhesive properties and facilitates their adherence to the inner surface of substances such as polyethylene, silicone, polyvinyl chloride (PVC), plastic, and copper tubing (7). They are ubiquitous in all types of watery environments, especially in stagnant water or wet soil. RGMs (and other mycobacteria) replicate well in wet or flooded soil but not in dry soil. They can be found in rivers, streams, lakes, ponds and springs (8). Strains of *M. fortuitum* and *M. chelonae*, among many others, were isolated from 430 of 683 (63%) surface water samples in one study (9), for example. Moreover, mycobacteriae have been consistently isolated in municipal and hospital water systems (10) as well as in hemodialysis centers (11,12). They have also been found to routinely persist in organic debris (i.e. biofilm) which is ever-present in pipes and filtration devices in potable water systems (7,8). Lastly, these ubiquitous organisms have been found to be extremely resistant to conventional water disinfection practices such as chlorination (13) as well as disinfectants used to decontaminate hospital equipment (14).

Pathogenic, rapidly-growing mycobacteria are a complex group of environmental organisms that cause human disease. There are now eight recognized taxonomic groups including five named (*M. fortuitum, M. chelonae, M. abscessus, M. smegmatis, and M. peregrinum*) and three, as yet, unnamed groups (15). Infrequently, they can cause non-cavitary pulmonary disease, especially in older adults. More frequently, they cause skin or deeper soft tissue infections, usually following trauma such as puncture wounds, open fractures, gun shot wounds and implantation of CV catheters (15). Septicemia can follow these cutaneous infections, especially in: a) immunosuppressed patients, b) in the post-transplantation period, c) in patients receiving corticosteroid therapy, and d) in those suffering from chronic renal failure (16). Disseminated infections of hemodialysis patients with RGMs have also been reported. In one case report by Azadian *et al* (17), water softener resins from hospital and home dialysis machines were found to be contaminated by strains of *M. chelonae* and *M. fortuitum* which apparently originated in the hospital's water supply.

## Fort Sam Houston (FSH) and BAMC Water Systems

The FSH potable water system serves as the source of water for BAMC. The FSH system receives its source water from five wells drawing water from the Edwards Aquifer; the same aquifer which serves the city of San Antonio. There are 3 wells at Building #2194, the main water treatment plant and two additional wells at Building # 3190, an auxiliary plant. The raw water quality from the Edwards Aquifer remains relatively constant with the exception of hardness values which fluctuate depending upon the water level in the aquifer. Raw water at Fort Sam Houston is very hard, ranging from 255 to 325 mg/L of $CaCO_3$. The pH is typically 7.2-7.3 with 7.6 being the highest value ever recorded and 6.9 being the lowest value ever recorded. The temperature is constant at $78^0$F. All well water is disinfected with chlorine gas, fluoridated with hydrofluosilicic acid and dosed with sodium hexametaphosphate for corrosion control. Water treatment plant operators monitor finished water pH, free chlorine (disinfectant) residual, and fluoride leaving the water treatment plants and at the base of each of the two elevated 1-million gallon distribution system storage tanks once every four hours. Chlorine residuals leaving the storage tanks are typically within 0.75 - 1.5 mg/L free available chlorine (FAC).

Distribution system water quality is checked by Preventive Medicine (PVNTMED) while collecting weekly potable water samples for total coliform analysis. The PVNTMED checks FAC, pH, temperature, and fluoride levels at each of the week's total coliform sample locations. Distributed water FAC ranges from 0.2 - 2.2 mg/L with typical values near 1.5 mg/L. Distributed water pH ranges from 7.2 - 7.8. Distribution system pressures vary from 30 - 160 pounds per square inch (psi) depending upon the height of water in the storage tanks and the number of well pumps operating. The FSH Directorate of Public Works (DPW) pipe replacement program should improve distribution system pressures to ensure a minimum near 50 psi when complete later on in FY 99. The pipe replacement program began 7 years ago replacing the old asbestos-cement (AC) pipes to mitigate problems with frequent breakage. As many as three breaks a day occur in the old AC pipe system, increasing workload of the DPW and frequently leaving sections of FSH without water for several hours or longer.

It should be noted here that in July 1996, shortly after the new BAMC hospital opened (in April 96), the 12-inch main serving the hospital broke near its crossing at Salado Creek, draining the nearest storage tank. The BAMC was reportedly without water for at least several hours. Such a large main break inevitably caused reduced pressures within the system providing for contamination, including water-borne pathogens such as *Mycobacteria spp,* to enter into the potable water distribution system. It is unclear as to whether this was the exact cause of the RGM contamination within the hospital plumbing system, since RGM sampling has not been conducted in the past, nor have samples been collected within various radii of the hospital to determine whether or not it is a localized problem. Localization of infections provides little indication of the extent of RGM occurrence since the *Mycobacteria spp.* of concern are opportunistic pathogens, affecting only those with weak immune systems. A separate report providing additional detail on the FSH potable water system is available (18).

There are a number of potable water systems within the new BAMC hospital. All systems are maintained and operated by Johnson Controls Inc., the contracting company responsible for all utility operations within the new BAMC hospital. Figures 1 & 2 provide a general depiction of the hot water and softened water distribution systems within the hospital relevant to this evaluation. Treated water from the FSH distribution system enters the hospital through a 10-inch cast iron pipe that leads to three booster pumps which provide adequate pressure for all 7 stories of the BAMC hospital. Although this water is treated FSH water, it is herein referred to as "raw" water since it is the source water for the BAMC water treatment system.

A portion of the raw water flow to BAMC provides water to the outside irrigation systems, hose hook-ups, and mechanical room janitorial sinks. The remainder of the raw water is softened through three parallel cation exchange resin softeners, each capable of treating 250,000 gallons of water to 0 ppm hardness [expressed as calcium carbonate ($CaCO_3$) concentration] before requiring regeneration (Figure 3 illustrates one of the water softener units). In order to minimize corrosion to the copper plumbing system, the combined softener effluent is mixed with a small portion of the non-softened flow through an automatic metering valve (Figure 4 illustrates a metering valve) to provide a product water with a recommended hardness of approximately 100 ppm (19). This combined water, herein referred to as "softened" water provides the potable cold and hot water for the hospital. Several other flows from this main system are further treated for their individual intended uses, such as reverse osmosis and ultraviolet (UV) light disinfected water for the hemodialysis machines and reverse osmosis purified and deionized water for the laboratories.

It is important to note that, in addition to removing the hardness from the raw water, the softeners also remove any FAC, leaving water throughout the hospital plumbing system without disinfection capabilities. The lack of disinfectant residual for the first two years of operation provided ample opportunity for both pathogenic and nonpathogenic microorganisms to enter into and colonize the BAMC plumbing system. Since discovery of RGM in the potable water within the hospital in March 1998, Johnson Controls Inc. initiated disinfection (via injection of sodium hypochlorite) of the softened water system and began manual hyperchlorination on 13 May in an attempt to eliminate *Mycobacteria spp*. However, high fluctuations of flow from day-to-night made it impossible to maintain a consistent and elevated FAC throughout the hospital for a full

24 hours, and the intended hyperchlorination goal was not met. Upon completion of the EPICON team visit on 13 June 98, Johnson Controls Inc. was completing a contract for the installation of a flow-controlled sodium hypochlorite injection system with automatic feed rates based on FAC detections within the hospital. This flow-controlled system will facilitate hyperchlorination as well as maintenance disinfection of the hospital's potable water system.

## PURPOSES and CONCEPT of the INVESTIGATION

The objectives of and general approach to this EPICON investigation included:

1. During the period of 1 May 1997 thru 8 June 1998, define the nature and extent of RGM infections in BMT recipients and in a comparable group of immunosuppressed patients at BAMC.
2. Define specific time period(s) of increased incidence and specific high-risk patient populations within BAMC.
3. Define any potential associations with risk factors for RGM infection, to include medical procedures, underlying illnesses and potential water exposures.
4. Identify and culture potential environmental (water) sources of infection.
5. Compare clinical and environmental RGM isolates, characterizing genetic (DNA fingerprinting) homologies among confirmed cases and potential environmental sources.
6. Provide recommendations for the prevention and control of future RGM infections in high-risk patients to include, if necessary, modifications in existing infection control practices, patient-to-staff interactions, limitation of hospital water exposure(s), and/or further treatment of hospital water supply system.

## PROCEDURES and METHODS

### Medical Data Sources

1. Review of Background Information & Listing of Cases: Upon arrival of the EPICON team on 8 June, an initial medical briefing was conducted with the Chairman, Infection Control Committee, MAJ Robert Plemmons. Attending were also COL David Dooley, Chief, Infectious Disease Service, LTC Susan Fraser, Infectious Disease staff, and LTC Dana Gruber, Chief, Infection Control Service, BAMC. The reported cases to-date (13) were reviewed by MAJ Plemmons and a case definition was arrived at (same one used prior by Dr. Plemmons). An initial listing of cases was developed for review of the EPICON team by MAJ Plemmons and LTC Fraser. A summary of key events surrounding the outbreak was also prepared by MAJ Plemmons and discussed with EPICON team members (see Appendix A). A review of the control procedures established by the Infectious Disease Service and Infection Control Committee, BAMC, was also undertaken. Additionally, historical records were obtained for the number of BMT unit transplant procedures by fiscal year for the years FY93 to FY98 (i.e. Oct 92 to May 98). A comparison was made for RGM rates of infection (in %) at the BMT unit for the past 6 years in order to define better trends in RGM infections in time.

2. Review of Procedures & Infection Control Practices at the BMT unit: Individual interviews were held on 8 June with LTC Dana Gruber, Chief, Infection Control Service, as well as with MAJ Bethany Alexander, Head Nurse, BMT unit to review past & existing infection control practices at the BMT unit. Additionally, a walk-through visit of the BMT unit was made by COL Sanchez, MAJ(P) Nang, and Dr. Brundage, in coordination with Dr. Rickey Myhand, Chief, BMT unit, and MAJ Alexander. Existing BMT procedures were reviewed in detail and facilities were seen and photos taken. A walk-through of the adjoining stem cell laboratory section was made and procedures for stem cell harvesting, preparation and infusion reviewed in detail. Data on the dates, times, types (frozen versus gel) and number (i.e. bags) of stem cell transfusions, as well as the involved technicians' data for all 14 affected patients identified during this EPICON were obtained.

3. Review of Patient and Staffing Patterns at BMT unit & Heme-onc (Ward 6W): Individual interviews were held with MAJ Alexander, Head Nurse, BMT unit, and MAJ Awilda Meeks, ANC, Head Nurse, Heme-Onc Ward (6W) on 9-10 June. Data regarding staffing patterns between BMT unit (affected immunosuppressed population) and Ward 6W (unaffected immunosuppressed population) were compared for the period of January 1997 to May 1998 to examine any potential association with increased rates of RGM infections at the BMT unit. Patient-to-Staff ratios were compared by month (as well as total) between both locations.

4. Review of Mycobacteria Section (& other) Laboratory Records: A review of existing mycobacterial laboratory section culture and identification procedures was made by LTC Fraser in coordination with Ms. Concha Garza, Mycobacteriologist, BAMC. Possible sources of specimen contamination at the laboratory were investigated. In addition, a computerized summary of RGM isolates (*M. chelonae* and *M. fortuitum*) and common bacterial skin contaminants (*Staphylococcus aureus* and *S. epidermidis*) for the preceding 18 months (January 1997 to May 1998) was obtained. Distribution and rates (per 1,000 patients) for the BMT unit and Ward 6W were calculated as a "proxy" measure for assessing a possible breakdown in infection control precautions.

5. Review of Interventional Radiology Department Records: An interview was held on 10 June with MAJ Allen M. Johnson, Chief, Special Procedures, Department of Interventional Radiology, BAMC. An illustration of the types of central venous (CV) line catheters, placement procedures, and listing of all CV line placements for the period of January 1997 to May 1998 was obtained. In order to assess possible staff-association(s) with RGM infections, the total number (and rates in %) of CV line catheter procedures performed in case patients (versus non-case patients) were compared for each of four radiologists involved.

6. Case-Control Study:

Based on the detection of a clear increased risk of RGM infection for patients sustaining BMT procedures, two sets of controls (i.e. noncases) were selected as follows. For the case-control study, the outbreak period encompassed the period May 1997 (onset of 1$^{st}$ case) to May 1998 (onset of last 3 cases). The case group consisted of a total of 14 cases (defined as 13 BMT recipients and one non-BMT recipient) retrospectively identified at BAMC who had documented, culture-proven, RGM infections during that period. The group of 46 controls was

randomly selected based on matching month of admission to each case trying to attain a 1:2 ratio (one "internal" control at the BMT unit, one "external" control at the Heme-onc Ward).

To identify and quantify specific correlates of infection risk, RGM cases and noncases were compared with relation to demographic, medical, and procedure-related characteristics. Records of relevant hospitalizations of each RGM case and referent noncases were reviewed, and data was recorded on forms developed specifically for the investigation. Known and potential risk factors for infection were evaluated by calculating crude odds ratios (OR, 95% CI) for cases versus each set of controls (for dichotomous variables) and by comparing measures of central tendency (mean $\pm$ SE, median) for continuous variables. Multivariate logistic regression analysis was performed on medically (or statistically) "significant" variables after univariate analysis. Adjusted odds ratios (AOR, 95% CI) were determined to estimate the independent effects of "significant variables.

**Environmental (Water) and Laboratory Isolate Data Sources**

1. Review of Past & Present Water System Sampling at BAMC:

Initial briefings were held on 8-9 June by the EPICON team, Water Supply Management (WSM) Program members (Mr. Valcik, Mr. Brokaw & Ms. Filippelli) with, among others: 1) LTC Kenneth J. Tannen, Environmental Science Officer; 2) Mr. Roy Hirchak, Chief, Facilities Management Branch; 3) Mr. Ben Keeble, Project Manager, Johnson Controls Inc.; 4) Mr. Gerald Camden, Directorate of Public Works (DPW), FSH; and, 5) Mr. Ron Bishop & Mr. Frank Benavides, BAMC Safety Office. A review of the existing FSH and BAMC water distribution systems was made and engineering plans obtained. Records of water sampling maintained by the post's DPW and BAMC Preventive Medicine Services (PMS) were reviewed. A review of past available BAMC potable water analysis, specifically for *Mycobacteria spp.* contamination, was conducted in order to detect possible association(s) between the inhospital water consumption and/or exposure and the perceived relative increase in numbers of BMT patients with RGM infections.

Water sampling schemes before and after the RGM problem was detected (ca. October 1997) were compared. As a background to this investigation, the original potable water samples from the BAMC potable water system which were taken initially in February 1998 were found to be small in volume (32 samples-50 mls each). These initial samples had been supplemented by additional larger (1L) samples collected during the period of March through end of May 1998. Immediately preceding (5 June 98) and during the EPICON team's visit on 8-13 June 1998, additional, targeted water samples were taken to further elucidate or pin-point sources of potential mycobacterial contamination.

2. Mycobacterial Analysis at BAMC Laboratory:

Patients' as well as potable water samples from BAMC were subjected to mycobacterial culture at the Mycobacteria Section, BAMC Laboratory, by Ms. Concha Garza. Samples of water from sinks, showers and ice machines were obtained in sterile 50 ml or 1 liter containers. The volume of water obtained from ice roughly equaled 30 ml or 600 ml, respectively. The

entire water or melted ice samples were filtered using sterile 0.45 micron filters. The filter was vigorously washed with 2.0 ml of sterile distilled water and 0.2 ml of the filter washing was then plated unto non-selective and selective media for mycobacteria. A Bactec 12B vial was inoculated with 0.5 ml of filter washings, and then the entire filter was inverted and cultured unto a non-selective Middlebrook 7H11 agar plate. The plates were incubated at $37^0$C in a 5 to 7% $CO_2$ environment and the Bactec 12B vials were incubated at $37^0$C in a non $CO_2$ environment. The plates were read weekly for the presence of mycobacteria and for the growth of other microorganisms. The vials were tested for the presence of acid fast organisms twice-weekly for the first 3 weeks and weekly thereafter for 6 weeks. Suspected colonies of RGM were smeared and stained by the Kinyoun method (20). All colonies showing acid fast organisms were subcultured unto Lowenstein-Jensen slants for biochemical studies, identification and referral for DNA fingerprinting.

The majority of patient samples were referred from either the blood culture bench or the pyogen bench in the bacteriology laboratory. These isolates were stained directly by the Kinyoun method and inoculated unto Lowenstein-Jensen and Middlebrook agars for further biochemical testing, identification and referral for DNA fingerprinting. In one case, biopsy tissue from a patient's central venous (CV) catheter insertion site was submitted directly to the mycobacteriology laboratory for processing. This tissue was processed according to standard mycobacteriology methods (20), stained by the fluorochrome method, and inoculated unto selective agar and liquid media as outlined above.

3. Genetic (DNA) Fingerprinting of *Mycobacteria spp.*:

Analysis of patient and water sampling RGM isolates obtained at BAMC Mycobacteria laboratory section, were further evaluated by DNA fingerprinting techniques. This was done so the similarities between the molecular DNA composition of patient and water samples could be compared in order to examine a possible correlation between the hospital's potable water supply and these patients' infections. Polymerase chain reaction (PCR) restriction fragment length polymorphism (RFLP) analysis (PRA) and pulse-field gel electrophoresis (PFGE) was performed at the Department of Microbiology, University of Texas Health Center at Tyler (UTHCT) by Ms. Barbara A. Brown, MS, MT(ASCP)SM.

Submitted RGM isolates were identified to species level by standard methods (20) as well as by antimicrobial susceptibility patterns (21-24). DNA was prepared from cells harvested from agar slants containing isolates obtained from patients and water, according to the methods described in references 23 and 25. The PRA method was utilized to confirm the identifications of all RGM, and the PFGE pattern of each isolate was compared to those obtained from the other isolates (25,26). PFGE patterns were determined to be either unique or identical to one or more of the other submitted samples.

## RESULTS

### Medical Data

1. Review of Background Information & Listing of Cases:

After review of all hospitalization and clinical microbiology records with the BAMC staff, 14 RGM cases were identified among immunosuppressed patients for the period of May 1997 to May 1998. See Table 1. Of these cases, all but one had received autologous peripheral blood stem cell infusions on the BMT unit; the remaining case (patient # 5) involved a patient with myelodysplastic syndrome treated at the Heme-onc ward and who developed septic arthritis (*M. fortuitum* isolated from a knee effusion while in the hospital). Of the remaining 13 patients who were admitted to the BMT unit, 11 had a primary diagnosis of breast cancer and 2 suffered from non-Hodgkins lymphoma. A total of five (36%) of these 14 patients sustained *M. chelonae* infections, 5 (36%) had *M. fortuitum*, 2 (14%) had *M. abscessus* and 2 (14%) had mixed types (*both M. chelonae & M. fortuitum* species). In 8 (57%) of the 14 cases a preceding central venous (CV) line catheter or tunnel infection was documented. In all but one case infections were succesfully treated; one patient (# 8) died of causes unrelated to her RGM bacteremia in March 1998.

See Table 2. Records of the BAMC BMT unit revealed that, from October 1992 through October 1996, there were no RGM infections associated with 158 bone marrow transplants [incidence rate (IR) = 0.0 infections per 100 BMTs, 95% CI = 0.0-2.3]. During fiscal year 1997, there were 3 infections associated with 90 transplants (IR = 3.3 per 100 BMTs, 95% CI = 0.7-9.7). A significant increase was noted for the period of October 1997-May 1998 when there were 10 infections associated with 75 transplants (IP = 13.3 per 100 BMTs, 95% CI = 6.4-24.5). By comparison, the BMT program at the University of Minnesota Hospital reported 7 RGM infections among 2,241 BMT recipients over a 20-year period (IR = 0.3 per 100 BMTs, 95% CI = 0.1-0.6) (3). In two other non-military case reviews, no RGM infections were diagnosed among 682 (IR = 0.0 per 100 BMTs, 95% CI = 0.0-0.5) and 90 (IR = 0.0 per 100 BMTs, 95% CI = 0.0-4.1) BMT patients (4,5). In addition, no cases of RGM infections had been reported by BMT unit officials at the Audie L. Murphy Memorial Veterans Hospital in San Antonio. Thus, BAMC's recent BMT-related RGM experience markedly varied from its own prior and from others' reported experiences.

It should be noted that the BMT unit patients at the new BAMC (opened in April 1996) were drinking regular tap water for the period of April 1996 to April 1998. As an initial control measure, BAMC authorities had placed BMT unit patients to a bottled water drinking policy with no apparent abatement of the problem (e.g., patients # 11-14 sustained their infections after this change). Subsequently in early May 1998 a decision was made to have BMT patients bathe in bottled water and to put planned BMTs on hold. Hyperchlorination of the BMT unit water was accomplished on 14-15 May; growth of RGM species was also detected after this measure and the BMT unit was closed on 18 May 1998.

2. Review of Procedures and Infection Control Practices at the BMT unit:

Infection control practices in the BMT unit were followed according to guidelines published by the Infection Control Service, BAMC. All BMT unit inpatients have private rooms, with private sink and toilet. A shower room with 2 showers is available for bathing. Until mid-May 1998, inpatients were allowed to wash their hands in, shower in and drink the hospital tap water. CV line catheters and dressings were allowed to become wet when showering, but, dressing changes were performed shortly after bathing for all patients. The shower room was cleaned thoroughly after each patient use, and each private room was cleaned on a daily basis and then thoroughly after the patient's discharge from the hospital.

All health care providers were instructed to wear gloves when performing dressing changes, manipulating intravenous tubing, flushing lines or catheters, and when assisting patients with any wound care, bathing, or when handling urine or fecal matter. At every sink a 2% chlorhexidine gluconate handwashing solution is available. The plastic containers containing this solution are completely replaced when empty. Providers are instructed to wash their hands before and after every patient contact. Adherence to glove use and handwashing policies was found to be high.

There were no multi-use vials present on the ward for administration of drugs or narcotics. Drugs were prepared for each patient individually by the Heme-onc ward or inpatient pharmacies, and narcotics or other controlled substances were always administered from single-use vials. Potential contamination of stem cell (SC) infusion bags during SC bag warming was noted to occur; dye tests performed during immersion of stem cell bags in dyed water showed contamination of the infusion port during removal of the bag's protective cap. Use of sterile water for SC infusion bag warming was immediately adopted during the first week of June 1998. Despite this deficiency, a preliminary comparison of BMT unit cases and noncases with respect the mean number of stem cell bags infused, and medical technician involved in SC bag warming, revealed no clear associations.

3. Review of Staffing Patterns at the BMT Unit and Heme-onc ward (6W): See Table 3. Staffing patterns (patient-to-staff) were examined for both wards taking care of patients at high risk of RGM infections (e.e., immunosuppressed) for the period of January 1997 to May 1998. No differences were noted in staffing ratios. Overall an average of 8.7 patients per staff were taken care of at the BMT unit compared to a ratio of 10.5 patients per staff at the Heme-onc ward.

4. Review of Mycobacteria Section Laboratory Records: See Table 4 and Figure 5. During the period of May 1997 to May 1998 the RGM infection rates (per 1,000 patient-days) were found to be nearly 30 times higher (3.26 per 1,000 patient-days) for BMT unit patients as compared to only a rate of 0.12 per 1,000 patient-days for Heme-onc patients. Staphylococcal infection rates, however, were only slightly higher among Heme-onc than BMT unit patients (BMT rate of 1.26 per 1,000 patient-days compared to a Heme-onc rate of 2.32 per 1,000 patient-days). In addition, no breakdown in infection control procedures were detected at the BMT unit. Thus, the increased rate of RGM infections among BMT unit patients did not seem to reflect a predisposing breakdown of infection control diligence.

5. Review of Interventional Radiology Department Records:

During the period of January 1997 to May 1998, nearly all BMT and approximately three-fourths of Heme-onc ward patients had CV catheters placed to secure venous access for long-term intravenous medications. Four different radiologists surgically inserted CV catheters (n=68) in BMT patients; however, no radiologist inserted relatively more CV catheters of RGM cases than noncases (see Figure 6). BMT unit patients (both cases and noncases) were more likely than Heme-onc patients to have CV catheters with 3 internal channels ("triple lumen"), and most triple-lumen catheters of BMT patients were supplied by a single manufacturer ("company A", see Figure 7 for photo). However, we found similar proportions of BMT cases and noncases had "company A" brand triple-lumen CV catheters; 10 (71%) of 14 BMT cases and 17 (74%) of BMT noncases (74%) had these CV catheters placed by radiology staff. See Table 5. Thus, there were no associations between RGM infection risk and either type or manufacturer of or the physician who inserted the CV catheters of BMT patients.

6. Case-Control Study:

See Table 5. Comparison of BMT unit cases and controls: Among BMT patients, RGM cases were slightly older, more often Caucasian, more likely to have intercurrent chronic illnesses, and less likely to smoke than noncases. The hospitalizations of cases were also longer than noncases, and during their hospitalizations, cases had more days of severe neutropenia (less than 600 WBCs/$mm^3$) and had a higher mean maximum temperature than noncases. Also, 85% of BMT cases developed positive blood cultures during hospitalization compared to only 31% of noncases ($P < 0.05$). Finally, more BMT unit cases than noncases were seen to develop signs of central venous (CV) catheter inflammation (at the insertion site and/or the subcutaneous tunnel) although the difference was not statistically significant.

See Table 5. Comparison of BMT unit cases and Heme-onc controls: Among BMT cases and Heme-onc controls, cases were more likely to be female, to have a history of breast cancer, to have evidence of mucositis (inflammation and erosion of mucosal surfaces) during hospitalization, and to have signs of CV catheter inflammation.

See Table 6. On multivariate analysis that included cases and both internal and external controls (adjusted for effects of age, gender and race) only central venous (CV) catheter inflammation (AOR=7.63, 95% CI 1.32-44.08) and a positive blood culture (AOR=6.38, 95% CI 1.06-38.39) during hospitalization were statistically significantly correlated with RGM infection risk. There were no associations found between RGM infection risk and either type of, manufacturer of, or the physician who inserted the CV catheters of BMT unit patients.

**Environmental (Water) and Laboratory Isolate Data**

1. Review of Past & Present Water System Sampling at BAMC:

Table 7 summarizes pertinent events affecting the BAMC potable water system and discovery of *Mycobacteria spp.* in the water. In summary, of a total of 32 water samples collected from the BMT unit (mainly from taps, showers, drinking fountains, and ice machines) in February 1998, none were positive for mycobacteria. However, all 3 samples collected in March, 24 of 30 samples collected in April, and all 27 samples taken in May were positive with concentrations of mycobacteria also increasing between March and May 1998. Table 8 shows a summary of the potable water's RGM analyses performed up to 10 June 1998 as well as the conclusions that can be arrived at from these results.

Repeated sampling performed on March through May 1998 found an increased number of samples positive for mycobacteria. However, it is important to note that it is possible that the *Mycobacteria spp.* could not be detected previously due to the small water sampling sizes (i.e., water sampling size was increased from 50 ml to 1 Liter in March 1998). Nevertheless, water samples from throughout the hospital, at the point of entry to BAMC, and from BAMC's water softener units (including resin, effluent and backwash) were positive for RGMs. In contrast, untreated water from the aquifer that serves FSH (and much of central Texas) and finished water from the main post plant were negative for mycobacteria.

Concomitant water mycobacterial culture, PCR RFLP and pulse-field gel electrophoresis (PFGE) DNA fingerprinting revealed that several patient isolates were similar to water sample isolates recovered at the same time from the BAMC potable water system (see Tables 9 & 10). Thus, it appeared that the water from the main post treatment plant was becoming contaminated in the pipeline between the main post and the hospital (or possibly at its point of entry into the hospital). It is also very likely that the BAMC's system of three water softeners served as an amplifying mechanism for maintenance of RGMs within the hospital's potable water supply.

Initial repeated attempts at hyperchlorination of BAMC's water system during a 3-month period (March to May 1998) were relatively unsuccesful in eradicating mycobacteria. Subsequent efforts (in June through November 1998) utilizing superheating and hospital-wide hyperchlorination were temporarily succesful in controlling the problem. Cultures of water collected one week after hospital-wide hyperchlorination on 21-22 November 1998 showed temporary eradication of mycobacteria from the water system for a period of up to 5 months (R Plemmons, personal communication). Subsequent sampling of same water points performed in April 1999, however, showed heavy growth of RGMs. Thus, it appears that the eventual probable solution may reside in the installation of ultraviolet (UV) light and/or additional filters for the water that serves the high-risk patients in the BMT unit and Heme-onc ward.

It should also be noted that, since the initial EPICON investigation, an additional BMT unit patient was found to be RGM-positive in December 1998 (R. Plemmons, personal communication). However, this patient had showered at the Fisher House while staying at FSH and his RGM isolate matched one of the Fisher House's water samples by DNA fingerprinting. Thus, he probably acquired infection from exposure to shower water outside of the hospital.

Ongoing efforts continue to be monitored by BAMC and USACHPPM staff to address this problem.

2. Mycobacterial Analysis at BAMC Laboratory:

Between May 1997 and May 1998, 13 BMT unit and 1 non-BMT unit (Heme-onc ward) inpatients had documented sterile site infections with RGM (see Table 1). A total of 16 isolates from blood, tissue and CV line catheters were recovered; data for fingerprinting analysis was obtained from 15 of the 16 isolates. The remaining isolate not examined came from a patient (patient # 14) who was transferred from the BMT unit at BAMC to William Beaumont Army Medical Center (WBAMC) for follow-up. The original report from the BAMC lab identified it as growth of *Nocardia spp.* and *M. chelonae*. The presumptive *M. chelonae* isolate mailed to BAMC lab was not viable upon arrival, however, it was strongly acid fast and the patient's clinical history and positive response to clarithromycin therapy were both highly consistent with a diagnosis of an RGM infection.

Based on the BAMC lab initial identification, the 14 patients' isolates were distributed as follows: five (36%) of these patients sustained *M. chelonae* infections, 5 (36%) had *M. fortuitum*, 2 (14%) had *M. abscessus* and 2 (14%) had mixed types (growth of both *M. chelonae* & *M. fortuitum* species). Thirteen of these 14 cases had received autologous peripheral blood stem cell infusions at the BMT unit; the remaining patient (patient # 5) had been admitted to the Heme-onc ward for a myelodysplastic syndrome.

3. Genetic (DNA) Fingerprinting Analysis of Isolates:

See Table 9. Further identification of the 15 isolates at UTHCT lab identified them as 8 *M. abscessus*, 4 *M. mucogenicum*, and 2 as *M. fortuitum*. Two of the eight *M. abscessus* isolates came from 2 different patients (patients # 3 & 8) and were identical by PFGE pattern. In addition, 3 of 8 *M. abscessus* isolates came from 3 different patients (patients # 6,7 & 13) and were all identical to each other and identical to the two *M. abscessus* isolates recovered from cold tap water in the BMT unit in March 1998. The remaining 3 *M. abscessus* isolates came from 3 different patients (patients # 9,10 & 12). The PFGE pattern of 2 of these 3 was found to be unique (the 3rd isolate was not tested).

Two of the 4 *M. mucogenicum* isolates came from 2 different patients (patients # 1 & 2) and were identical by PFGE pattern. The other 2 isolates (patients # 8 & 11) were unique. Also, the 3 *M. fortuitum* isolates recovered from patients # 4, 5 & 9 were unique by PFGE pattern. The three control (non-BMT unit) isolates obtained from patients from other areas of the hospital (2 sputum, 1 aspirate of neck mass) also had unique PFGE patterns which were unrelated to any of the isolates from BMT unit patients during our investigation.

We were able to recover isolates of *M. abscessus* and *M. fortuitum* from several samples of water taken on 10 June 1998 at the time of the EPICON team visit. These are outlined in Table 10. A total of 14 positive cultures out of 8 samples collected from several areas of the BAMC water system were detected. These included samples from the BMT unit patient room

(n=1), 1st floor bathroom faucet cold water (n=2), backwash rinse water from softener # 1 (n=1), water effluent from all 3 water softeners (n=8), and resin from water softener # 1 (n=2). One of the *M. abscessus* water isolates (Id # 1268-2) was found to be identical by PCR RFLP analysis (PRA) to the organism recovered from 3 of the patients and two water samples which were collected during the period of November 1997 to April 1998. See information listed for patients # 6, 7 & 13 in Table 9.

## DISCUSSION

### Medical Data

The medical and epidemiologic data collected during this investigation clearly documented a significantly increased rate of rapidly-growing mycobacterial (RGM) infections at Brooke Army Medical Center (BAMC) between May 1997 and May 1998. The increased risk affected almost exclusively BAMC bone marrow transplant recipients. During this high-risk period, the BAMC potable water system was contaminated with RGMs and, as time progressed, the level of contamination became more widespread than originally thought of. During this period, rates of other nosocomial infections, such as *S. aureus* and *S. epidermidis*, were comparable on the bone marrow transplant (BMT) unit and hematology-oncology wards. There was no evidence of a significant breakdown of infection control practices on the BMT unit. Thus, the increased rate of RGM infections among BMT unit patients did not seem to reflect a predisposing breakdown of infection control diligence.

We found that among BMT unit patients, RGM cases were slightly older, more often Caucasian, more likely to have intercurrent chronic illnesses, and less likely to smoke than noncases. Disseminated infections of hemodialysis patients with RGMs have also been reported in the past (1,2,17). Moreover, in one case reported by Azadian *et al* (17), a hospital-based RGM patient isolate was traced to water softener resins from hospital and home dialysis machines which were found to be contaminated by strains of *M. chelonae* and *M. fortuitum* which apparently originated in the hospital's water supply. The supposition that our patients acquired their infections by exposure to contaminated water is, therefore, very likely.

Our findings that the hospitalizations of cases were longer than noncases, and that cases also had more days of severe neutropenia (less than 600 WBCs/$mm_3$) and had a higher mean maximum temperature than noncases is very important. This would seem to indicate a longer time period at-risk for RGM cases while at BAMC.

Case-control study data seemed to indicate that central venous (CV) catheter site inflammation [adjusted odds ratio (AOR)=7.63, 95% CI 1.32-44.08] and the presence of positive blood cultures during hospitalization (AOR=6.38, 95% CI 1.06-38.39) were the only 2 factors which could be identified as possibly associated with RGM infection. There were no associations found between RGM infection risk and either type of, manufacturer of, or the physician who inserted the CV catheters of BMT unit patients. RGMs have been documented to be a frequent cause of skin or deeper soft tissue infections, usually following trauma such as puncture wounds, open fractures, gun shot wounds and implantation of CV catheters (15).

Septicemia can follow these cutaneous infections, especially in: a) immunosuppressed patients, b) in the post-transplantation period, c) in patients receiving corticosteroid therapy, and d) in those suffering from chronic renal failure (16). Thus, the associations with CV catheters and blood-borne infections found in our case-control study probably represent true associations.

**Environmental (Water) and Laboratory Isolate Data**

Biofilms in potable water: Potable drinking water is not sterile, i.e., free of microorganisms. Effective treatment generally removes pathogenic organisms to provide water that is safe for consumption. However, the non-sterile drinking water contains microorganisms that may colonize the surfaces with which it comes into contact. Ineffective disinfectant residuals are often a likely factor in colonization. These colonizations are referred to as "biofilms" and are typically made up of bacteria which are not normally pathogenic to humans. Sometimes, however, pathogenic bacteria such as *Klebsiella spp.*, *Escherichia coli*, some *Pseudomonas spp.*, and *Legionella spp.*, and opportunistic pathogens like *Mycobacteria spp.*, as well as other organisms like protozoa (amoebas), parasites (*Cryptosporidia* and *Giardia*) and enteroviruses have been detected (27). These pathogenic microorganisms enter into the drinking water system in one of five ways: 1) breakthrough of the drinking water treatment system from the raw water; 2) leaks/breaks in the water distribution system; 3) contaminated materials used in the water system such as filters or piping; 4) contamination with non-sterile air remaining in a pipe or holding tank; or, 5) backflow through cross-connections with non-potable sources (27).

*Mycobacteria* in biofilms:

Numerous studies have been performed on the effects and control of biofilms in drinking water distribution systems (7,27-29). One study in particular focused on *Mycobacteria* in biofilms (7). This study indicated that solid/liquid interfaces (such as wound filter media or softener resins) are sites of selective enrichment for *Mycobacteria* since their high degree of cell wall hydrophobicity and non-flagellate structure cause increased adhesion to such solid surfaces. According to the study, biofilms should be considered potential sources for opportunistic pathogens (opportunistic - generally cause illness to only the severely immunocompromised or when given direct access to bloodstream, such as through surgery or traumatic wounds) such as *M. kansasii*, *M. chelonae*, and *M. fortuitum* (7). Surfaces with a carbon source and hydrophobicity that experience a minimum degree of flow to provide nutrients to the immobilized bacteria provide the best homes for *Mycobacteria* colonization (7). Several locations within the BAMC hospital (the 3 softeners, all water filters to ice machines, reverse/osmosis membranes, any fiber-glass-lined hot water heaters, and any non-metal plumbing fixtures) meet this criteria and provide excellent areas for the *Mycobacteria* to colonize and proliferate in the absence of control measures (i.e., no disinfectant residual for 2 years).

Control of the *Mycobacteria* presents an interesting challenge as it is more resistant to common disinfectants than most bacteria and certain strains of *Mycobacteria* (*M. chelonae*) are more resistant to thermal treatment than *Legionellae* (14,30-33). Additionally, susceptibility to the various disinfectants and even heat treatment vary among the different species. Success of the treatment measures employed in reducing *Mycobacteria* can be measured through a series of analyses for *Mycobacteria* in pre- and post-treatment water samples. The heterotrophic plate

count (HPC), an assessment tool for defining the extent of biofilm populations within a distribution/plumbing system, could be used to monitor increasing biofilm organisms that may include *Mycobacteria.* A long-term HPC monitoring program could provide an assessment of continued *Mycobacteria* control within BAMC once the current contamination episode is remedied.

Review of potential *Mycobacteria* control methods:

Several studies have been conducted that confirm the relative resistance of *Mycobacteria* to chemical disinfectants (7,14,30,31). One study compared the relative thermal resistance of various species of *Mycobacteria* (33). As part of our investigation, several environmental and hygiene experts were contacted regarding control and eradication of *Mycobacteria* from potable water systems (47,48,50). The paragraphs below summarize available information on the ability of four disinfection options to minimize/control *Mycobacteria* in potable water.

Table 11 compares the estimated capital and operating costs of 3 methods that would require a capital equipment purchase. Reverse osmosis and other ultra-filtration methods were not considered due to the preference by *Mycobacteria* to colonize on membranes used in these processes. Additionally, reverse osmosis product water would likely be too corrosive to the hospital plumbing system(s). Ozone, although the most powerful disinfectant used in water treatment, produces biodegradable organic matter in treated water, which may further stimulate the growth of opportunistic pathogens still lurking within the distribution system (7,8,45). In addition, the lack of providing a residual, makes ozone an unlikely choice for centralized treatment unless all post-treatment hospital plumbing was thoroughly cleaned, disinfected and protected from cross-connections.

- Potable Water Treatment Options for BAMC:

1. Use of chlorine treatment (free and combined):

The use of chemical disinfectants provides perhaps the most convenient control method for BAMC since all of the equipment is already in place. However, chlorine residuals, both free and combined, and contact times used in commonly-accepted disinfection practices may not be effective against several *Mycobacteria* species. Studies show FAC concentrations of up to 1 mg/L and a 24-hr contact time do not effectively control *M. avium* in public water supply systems (35). Strains of *M. fortuitum* and *M. chelonae* have been shown to survive contact with 0.7 mg/L of FAC for over 60 minutes with less than a 2-log total reduction. By comparison, *M. fortuitum* strains survived a 60-minute contact time with 2.0 mg/L FAC (14).

Another study demonstrated the even greater resistance of the various species of *Mycobacteria* to combined chlorine residuals (i.e. chloramines). Table 12, extracted from reference 36, summarizes the results of one particular study. This provides useful information, showing the *M. avium* complex (*M. avium* 723, *M. avium* 743 and *M. intracellulare*) to be the most resistant species to chemical disinfection. *M. chelonae* was the most resistant among the remaining non-tuberculous species (36).

Using table 12, and assuming that FAC does inactivate *Mycobacteria* more effectively, disinfection procedures used to control *Legionella* outbreaks in hospitals (5.0 mg/L FAC for 24 hours) should be helpful in inactivating the biofilm within the BAMC hospital (37,38). However, routine disinfection via chlorination at levels below 5 mg/L, or at 5 mg/L without providing the necessary contact time (that is, at least 12-24 hours of contact time) may not prevent breakthrough of *Mycobacteria* entering the hospital and any resulting recontamination of the plumbing system. Additionally, it will not be possible to maintain such high residuals without greatly affecting the palatability of the drinking water.

2. Use of heat treatment (i.e. thermal destruction):

Since temperature plays an important role in the colonization by microbial organisms, alterations of normally occurring temperatures within water systems have been used to eradicate biofilm contamination of such organisms. Obviously, use of elevated temperature (known as superheating) as a control mechanism lends itself to treatment of building hot water plumbing systems. This method could easily be instituted using components (hot water boilers) which are already part of the BAMC water system. Although a proven method for controlling *Legionella* (37), few experiences have been documented on the effectiveness of these methods for controlling *Mycobacteria*.

One experimental study compared the relative resistance of the various species of *Mycobacteria* to varying temperatures, making an ultimate comparison with those temperatures used to control and eradicate *Legionella* in hot water plumbing systems (33). Applying the results of this study to thermal destruction of *Mycobacteria*, it can be assumed that *Legionella* eradication measures (heat and flush method >70$^0$C for at least 5 minutes) would be equally effective in eradicating most strains of *Mycobacteria*. Control methods, however, (maintenance of hot water storage to 60$^0$C and maintenance of hot water plumbing system to at least 50$^0$C) would only be adequate to control those species of *Mycobacteria* that are equally or more sensitive to temperature as *L. pneumophila*, such as *M. fortuitum* (33). Such measures may not be adequate for more heat-resistant species, such as *M. chelonae* and *M. avium* (33). Superheating the BAMC hot water system should eliminate any current *Mycobacteria* contamination within the system, but once temperatures are returned to normal, any *Mycobacteria* coming into the hot water system from the cold water make-up lines may again colonize and contaminate the hot water system. Additionally, there are real safety-related concerns regarding the potential scalding of patients, staff, and visitors exposed to superheated water. In that regard, precautions must be taken if the heat and flush method is used.

3. Use of Mixed Oxidant (MIOX®) technology:

The process of generating chlorine and hypochlorite ions electrolytically has been used since the late 1800's. The process has recently been revisited and new technologies are capable of creating a mixed-oxidant disinfectant even more powerful than chlorine or hypochlorite alone (42). Mixed-oxidant disinfection technology uses rock salt and a patented electrolytic cell (manufactured by the MIOX® Corporation) to produce an aqueous mixed-oxidant solution consisting primarily of chlorine with smaller amounts of chlorine dioxide and ozone. The

oxidants at the anode are injected into the raw water at the necessary dilution ratio to produce the desired FAC residual. The cathode product consists of sodium hydroxide and sodium hypochlorite. A side stream of water from the feed source is fed to a brine generator producing a 10 g/L NaCl solution that is feed stock for the electrolytic cell (® MIOX is a registered trademark of MIOX Corporation, 5500 Midway Park Place NE, Albuquerque, NM 87109).

The process is depicted in Figure 7 and details published elsewhere (41,44). Although specific information is not available on required levels necessary to disinfect *Mycobacteria* using MIOX, there have been several studies indicating required measures to control *Cryptosporidium* and *Bacillus subtilis* spore (41-44). Both of these organisms are extremely resistant to chemical disinfectants, and *Cryptosporidium* is known as the most resistant. MIOX disinfection with 5 mg/L as FAC for 4 hours provides 3-log inactivation of *Cryptosporidium* (43). Using these studies as guidelines, MIOX at a level of 4 mg/L for 60-minute contact time (known to provide 4-log inactivation of *B. subtilis*, reference 45) should sufficiently control *Mycobacteria* in potable water. Without exact information on MIOX disinfection of *Mycobacteria*, use of MIOX would likely require confirmatory sampling and resulting adjustments to treatment levels to provide the most cost-effective protection. Benefits to using MIOX over other chemical disinfectants (chlorine) include the reduced contact time required, less disinfection by-product formation and less taste and odor complaints, even with the higher residuals required to control *Mycobacteria* (42,44).

4. Use of Ultraviolet (UV) light:

Ultraviolet light treatment of drinking water involves the direct exposure of the water stream to ultraviolet light, damaging the nucleic acids of microorganisms, thus preventing them from propagating or remaining active (39). Research has shown that the optimum UV light wavelength range for bactericidal effect is between 250 nm and 270 nm with maximum biocidal effects occurring at 253.7 nm. Dosages of UV light that effectively inactivate a microorganism (measured in $\Phi Ws/cm^2$) varies per organism. Guidelines for the use of UV light for water disinfection, set by the U.S. Department of Health, Education, and Welfare in 1996, require a minimum dose of 16,000 $\Phi Ws/cm^2$ at all points throughout the disinfection unit. Most manufacturers size units to provide a minimum of 30,000 -35,000 $\Phi Ws/cm^2$. This dosage is known to provide 6-log reduction of several bacteria and a 4-log reduction of hepatitis A and poliovirus in potable water treatment (39).

An independent table-top study done on UV disinfection of Coliphage MS-2, a conservatively resistant non-pathogenic virus, required dosages between 64,000 and 93,000 $\Phi Ws/cm^2$ for a 4-log inactivation (49). Although there is no specific dosage information available for the *M. chelonae* and *M. fortuitum* spp., manufacturer's data shows dosages of 10,000 $\Phi Ws/cm^2$ are necessary for destruction of *M. tuberculosis*. Using these available studies and dosages, the typical dose of 30,000 $\Phi Ws/cm^2$ should be adequate for control of *M. chelonae* and *M. fortuitum*. Without exact dosage information, however, *Mycobacteria* samples would be required to determine if the 30,000 $\Phi Ws/cm^2$ dosage is adequate.

## RECOMMENDATIONS

1. The following medical control recommendations were made on 12 June 1998 (exit brief):

    a. The BAMC Infection Control Committee should establish a multi-disciplinary team to coordinate, track, and document case reports, water disinfection procedures and additional (future) interventions.

    b. BAMC's Laboratory should develop the capability to quantify mycobacteria in water samples in order to better support a comprehensive RGM surveillance program. If necessary, external laboratory support should be obtained.

    c. Continue surveillance for RGM-infected cases among immunosuppressed patients, especially at the BMTU ward, for a period of 3-4 months following the implementation of Stage 1 and 2 water treatment recommendations below.

    d. Consider the relocation of bone marrow transplant patients from the Hematology-Oncology ward (6W) back to the BMTU (ward 5N). Continue water restriction (i.e. no showering, bottled water use only for drinking/washing) precautions in place among BMTU patients until Stage 1 & 2 of water treatment recommendations have been completed and a 3-4 month period free of RGM-associated infections is documented.

    e. Consider the implementation of additional disinfection control measures at the BMTU, such as the use of alcohol for handwashing (instead of faucet water). The use of alcohol (or other high-level disinfectant) is especially important prior to the manipulation of any central venous (CV) catheter or peripheral IV lines.

    f. Consider the use of sterile water (instead of tap water) for the warming of frozen stem cell bags prior to infusion in BMT patients. Additionally, during the bag warming procedure, avoid direct immersion of bag ports into the water to avoid potential contamination of infusion bag/port.

2. The following recommendations for control of *Mycobacteria* in the BAMC potable water system were made on 12 June (exit brief) and subsequently updated on 16 July and 19 November 1998:

    a. It should be stressed that the potable water used in a hospital need not be sterile. Rather, control of densities of microbial populations appears to be a more adequate goal in providing protection to hospital consumers. Studies on the requirements of sterile water for dialysis processes (a more common vehicle for mycobacterial-induced illnesses), concluded that bacterial "contamination" in the incoming water (hospital water) and of the dialysate fluids should be kept to levels less than 1,000 total organisms/ml (46).

b. Since the exact level of control required to minimize infections from *Mycobacteria* in potable water is not known, a staged approach to recommendations for control are provided for BAMC. Additionally, control measures are presented for both the hot and cold water systems since they are independent plumbing systems. Immediate action needs to be completed to decontaminate (i.e., elimination of the biofilm) within the plumbing systems serving immunocompromised patients susceptible to *Mycobacteria* infections. These are Stage 1 recommendations. Further actions address reduction of *Mycobacteria* populations within the entire hospital. These are Stage 2 recommendations.

c. Both **Stage 1 and Stage 2 recommendations must be completed** to address the current *Mycobacteria* contamination of potable water within the BAMC water system. If these measures do not provide adequate control of RGM infections from potable water, localized treatment for affected wards (Stage 3 recommendations) and eventually whole hospital treatment (Stage 4 recommendations) **may be** required. The success of the control measures should be based on documented elimination of RGM infections in patients as explained in recommendations 1c. & 1d. above.

d. After decontamination, the institution of a persistent chlorine residual (started 13 May 1998) may provide enough control of *Mycobacteria* populations to meet this intent. A long-term HPC monitoring program throughout BAMC will provide information on the continued control of biofilm bacteria which should, in turn, provide information on the continued control of *Mycobacteria*.

e. The following **Stage 1** recommendations constitute **immediate actions** to decontaminate the BMTU and Hematology-Oncology wards' plumbing systems to protect immunosuppressed patients at high risk:

(1) Hyperchlorinate the BMTU and Hematology-Oncology wards' soft water systems using the centralized chlorination system in the central energy plant (CEP). Maintain an FAC residual of at least 5 ppm for 24 hours throughout all parts of the BMTU and Hematology-Oncology ward water systems. See Appendix B for specific guidance on hyperchlorination.

(2) Conduct thermal treatment of the hot water systems serving the BMTU and Hematology-Oncology wards. Raise the hot water system temperature from the normal system temperature of $43^0$C ($110^0$F) to $70^0$C ($158^0$F) and flush all water use points sequentially for at least 3 minutes. Then reduce the system temperatures to $60^0$C ($140^0$F) to provide continued control of Mycobacteria until decontamination of entire hospital (Stage 2) is completed.

(3) Sanitize the BMTU and Hematology-Oncology Ward ice machines and replace any associated filters (e.g., activated carbon).

(4) Collect soft (drinking) and hot water samples from BMTU and Hematology-Oncology Ward for mycobacterial analysis 24 and 48 hours after completion of "localized" decontamination measures [recommendations 2e(1) & 2e(2) above] to evaluate their effectiveness in eliminating gross contamination of Mycobacteria populations.

(5) Collect a set of "reference" cold and hot water samples for mycobacterial analysis from other exposure sites where no infection has been identified (e.g., the Guest House, Wilford Hall and other BMTU's in local area). These samples are to help establish a *Mycobacteria* population baseline/control goal.

f. The following **Stage 2** recommendations constitute **future actions** to decontaminate the entire BAMC water system, to be conducted over a period of a few weeks:

(1) Proceed with the replacement of the softener resin media. Sanitize the softener units in accordance with accepted criteria (e.g., American Water Works Association Disinfection Standards).

(2) Ensure centralized chlorination maintains uniform FAC residual entering the BAMC soft water system regardless of demand (flow) variations.

(3) Hyperchlorinate entire hospital system (at least 5 ppm for 24 hrs) as described in recommendation 2e(1) above for each BAMC soft water riser and associated plumbing systems.

(4) Sanitize **all BAMC** ice machines and replace any associated filters (e.g. activated carbon).

(5) Expand Preventive Medicine Service's total coliform monitoring program to include weekly HPC samples of water entering and leaving the BAMC centralized soft water treatment system and at least one rotating location within the BAMC soft water system.

g. The following **Stage 3** recommendations constitute additional actions if routine medical surveillance identifies additional cases of RGM infections among BMTU, Hematology-Oncology ward or other immunosuppressed patients in BAMC.

(1) Install localized treatment (either MIOX or UV) of soft water specifically for the BMTU and Hematology-Oncology wards.

(2) Install appropriate treatment (UV disinfection) on soft water makeup for the hot water systems serving the BMTU and the Hematology-Oncology wards.

(3) Collect soft and hot water samples for mycobacterial analysis from the BMTU and Hematology-Oncology wards to evaluate the Stage 3 control measures and from other appropriate BAMC locations. Adjust treatment system disinfectant doses as necessary to meet Mycobacteria population goal as established by reference samples [from Stage 1 recommendation in 2e(5) above]. Sample frequency should be weekly for three weeks. Surveillance should continue weekly or bi-weekly if further infections occur.

h. The following **Stage 4** recommendations constitute additional actions to protect the entire BAMC water system if infections continue after implementation of Stage 3 recommendations:

(1) Apply MIOX or UV treatment for the water supply at the point of entry to BAMC to control *Mycobacteria* from the Fort Sam Houston water distribution system. Implementation would be a significant engineering undertaking and will require a relatively long time (months/year) to accomplish.

(2) Consider installing "one-way flow" valves (e.g., double-check valves) at strategic locations throughout the BAMC soft water system to prevent return flow from any relatively unused areas where biofilms may proliferate.

(3) Conduct surveillance monitoring for *Mycobacteria* at representative soft and hot water locations throughout BAMC weekly for at least three weeks to evaluate the effectiveness of the Stage 4 improvement measures.

## REFERENCES


1. Ellison RT. Infections associated with bone marrow transplantation. *In* Gorbach SL, Bartlett JG, Blacklow NR (eds): Infectious Diseases. Philadelphia, WB Saunders, 1998, pp 1237-1242.

2. Sable CA, Donowitz GR. Infections in bone marrow transplant recipients. Clin Infect Dis, 1994; 18: 273-281.

3. Roy V, Weisdorf D. Mycobacterial infections following bone marrow transplantation: a 20-year retrospective review. Bone Marrow Transplantation 1997; 19: 467-470.

4. Navari RM, Sullivan KM, Springmeyer SC, et al. Mycobacterial infections in marrow transplant patients. Transplantation 1983; 36: 509-513.

5. Kurzrock R, Zander A, Vellekoop L, *et al.* Mycobacterial pulmonary infections after allogeneic bone marrow transplantation. Am J Med 1984; 77: 35-40.

6. Chapman JS. The ecology of the atypical mycobacteria. Archives of Environmental Health 1971; 22: 41-46.

7. Schulze-Robbecke R, Janning B, Fischeder R. Occurrence of mycobacteria in biofilm samples. Tubercle and Lung Disease 1992; 73: 141-144.

8. Collins CH, Grange JM, Yates MD. A Review: Mycobacteria in water. Journal of Applied Bacteriology 1984; 57: 193-211.

9. Viallier J, Viallier G. Inventaire des mycobacteries de la nature. Annales de la Societe Belge de Medicine Tropicale 1973; 53: 361-371.

10. Glover N, Holtzman A, Aronson T, *et al.* The isolation and identification of *Mycobacterium avium* complex (MAC) recovered from Los Angeles potable water, a possible source of infection in AIDS patients. International Journal of Environmental Health Research 1994; 4: 63-72.

11. Bolan G, Reingold AL, Carson LA, *et al.* Infections with *Mycobacterium chelonei* in patients receiving dialysis and using processed hemodialyzers. J Infect Dis 1985; 152: 1013-1019.

12. Carson LA, Bland LA, Cusick LB, Favero MS, Bolan GA, Reingold LA, Good RC. Prevalence of nontuberculous mycobacteria in water supplies of hemodialysis centers. Applied and Environmental Microbiology 1988; 54: 3122-3125.

13. Reasoner DJ. Pathogens in drinking water-are there any new ones? Original presentation at the Water Quality Technology Conference (WQTC) of the American Water Works Association (AWWA), Orlando, Florida, November 1991.

14. Carson LA, Petersen NJ, Favero MS, Aguero SM. Growth characteristics of atypical mycobacteria in water and their comparative resistance to disinfectants. Applied and Environmental Microbiology 1978; 36: 839-846.

15. Wallace RJ. Recent changes in taxonomy and disease manifestations of the rapidly growing mycobacteria. European Journal of Clinical Microbiology and Infectious Diseases (Current Topic:Review) 1994; 13: 953-960.

16. Wallace RJ, Brown BA, Onyi GO. Skin, soft tissue, and bone infections due to *Mycobacterium chelonae chelonae*: importance of prior corticosteroid therapy, frequency of disseminated infections, and resistance to oral antimicrobials other than clarithromycin. J Infect Dis 1992; 166: 405-412.

17. Azadian BS, Beck A, Curtis JR, *et al.* Disseminated infection with Mycobacterium chelonei in a haemodialysis patient. Tubercle 1981; 62: 281-284.

18. Memorandum, USAEHA, HSHB-ME-WR, 30 June 1994, subject: Potable/Recreational Water Quality Survey No. 31-24-G2UA-94, Fort Sam Houston, Texas, 18-28 January 1994.

19. Memorandum, USACHPPM, MCHB-AS-EH, 17 June 1996, subject: Water Quality Consultation No. 31-08-5422-96, Fort Sam Houston, Texas, 6-30 May 1996.

20. Metchok BG, Nolte FS, Wallace RJ. Mycobacterium. *In* Murray PR, Barron EJ, Pfaller MA, Tenover FC, Yolken RH (eds): Manual of Clinical Microbiology. Washington, DC, ASM Press, 1999, pp 399-437.'

21. Silcox VA, Good RC, Floyd MM. Identification of clinically *significant Mycobacterium fortuitum* complex isolates. J Clin Microbiol 1981; 14:686-91.

22. Steele LC, Wallace RJ. Ability of ciprofloxacin but not pipemidic acid to differentiate all three biovariants of *Mycobacterium fortuitum* from *Mycobacterium chelonae*. J Clin Microbiol 1987; 25:456-7.

23. Telenti A, Marchesi F, Balz M, et al. Rapid identification of mycobacteria to the species level by polymerase chain reaction and restriction enzyme analysis. J Clin Microbiol 1993; 31:175-8.

24. Wallace RJ, Brown BA, Silcox VA, et al. Clinical disease, drug susceptibility and biochemical patterns of the unnamed third biovariant complex of *Mycobacterium fortuitum*. J Infect Dis 1990; 163:598-603.

25. Steingrube VA, Gibson JL, Brown BA, et al. PCR amplification and restriction endonuclease analysis of a 65-kilodalton heat shock protein gene sequence for taxonomic separation of rapidly growing mycobacteria. J Clin Microbiol 1995; 33:149-53.

26. Wilson RW, Steingrube VA, Brown BA, et al. Clinical application of PCR-restriction enzyme pattern analysis for rapid identification of aerobic actinomycete isolates. J Clin Microbiol 1998; 36:148-52.

27. Schaule G, Fleming Hans-Curt. Pathogenic microorganisms in water system biofilm need biofilm sampling. Ultrapure Water, April 1997.

28. LeChevallier MW. Disinfection of biofilms in drinking water systems. Original presentation at the Water Quality Technology Conference (WQTC) of the American Water Works Association (AWWA), Denver, CO, November 1997.

29. Characklis WG. Project summary. In Characklis WG: Bacterial Regrowth in Distribution Systems. AWWA Research Foundation, Denver, CO, January 1988, pp xv-xxix.

30. Vess RW, Anderson RL, Carr JH, Bond WW, Favero MS. The colonization of solid PVC surfaces and the acquisition of resistance to germicides by water micro-organisms. Journal of Applied Bacteriology 1993; 74: 215-221.

31. Norton, CD, LeChevallier MW, Falkinham III JO. The Occurrence and Control of *Mycobacterium avium* Complex. Original presentation at the Water Quality Technology Conference (WQTC) of the American Water Works Association (AWWA), Denver, CO, November 1997.

32. Drinking Water Inspectorate Fact Sheet - *Mycobacterium avium* complex. AWWA Research Foundation, Denver, CO, Fact Sheet No. 7: Issue No. 1, March 1997.

33. Schulze-Robbecke R, Buchholtz K. Heat susceptibility of aquatic Mycobacteria. Applied and Environmental Microbiology 1992; 58: 1869-1873.

34. vonReyn CF, Maslow JN, Barber TW, Falkinham III JO, Arbeit RD. Persistent colonisation of potable water as a source of *Mycobacterium avium* infection in AIDS. Lancet 1994; 343: 1137-1141.

35. Pelletier PA, duMoulin GC, Stottmeier KD. Mycobacteria in public water supplies: comparative resistance to chlorine. Microbiological Science 1988; 5: 147-148.

36. Pelletier PA, Carney EM, duMoulin GC. Comparative resistance of *Mycobacterium avium* Complex and other non-tuberculous mycobacteria to chloramine. Original presentation Annual American Water Works Association (AWWA) Conference, Philadelphia, PA, June 1991.

37. Allegheny County Commissioners, Health Department and Board of Health. Approaches to Prevention and Control of Legionella Infection in Allegheny County Health Care Facilities, Allegheny County Health Department, Pittsburgh, PA, 1997.

38. Muraca PW, Yu VL, Goetz A. Disinfection of water distribution systems for Legionella: a review of application procedures and methodologies. Infection Control and Hospital Epidemiology 1990; 11(2): 79-88.

39. United States Environmental Protection Agency (USEPA). Ultraviolet Light Disinfection Technology In Drinking Water Application - An Overview, EPA 811-R-96-002, Office of Water, September 1996.

40. USEPA. Very Small Systems Best Available Technology Cost Document, Office of Ground Water and Drinking Water. Report by Malcolm Pirnie, Inc., 1993.

41. Herrington RE, Bradford WL. Pilot study report mixed-oxidant disinfection system at Greenfield, Iowa. Original presentation at the Water Quality Technology Conference (WQTC) of the American Water Works Association (AWWA), Denver, CO, November 1997.

42. Crayton C, Camper A, Warwood B. Evaluation of mixed-oxidants for the disinfection and removal of biofilms from distribution systems. Original presentation at the Water Quality Technology Conference (WQTC) of the American Water Works Association (AWWA), Denver, CO, November 1997.

43. Venczel L, Arrowood M, Hurd M, Sobsey M. Inactivation of *Cryptosporidium parvum* oocysts and *Clostridium perfringens* spores by a mixed-oxidant disinfectant and by free chlorine. Applied and Environmental Microbiology 1997; 63:1598-1601.

44. Product information from MIOX Corporation, 5500 Midway Park Place, NE, Phone: (888)MIOX-H20, 1998.

45. Daniel PA, Leonard SL. Maximizing risk reduction: applications and limitations. Original presentation at the Water Quality Technology Conference (WQTC) of the American Water Works Association (AWWA), Boston, MA, November 1996.

46. Jones DM, Tobin BM, Harlow GR, Ralston AJ. Bacteriological studies of the modified Kiil dialyzer. British Medical Journal 1970; 3: 135-137.

47. Phone conversation between Mr. John Brokaw, USACHPPM, and Dr. Don Reasoner, USEPA National Risk Management Research Laboratory, 5 June 1998, subject: General Characteristics of Mycobacteria.

48. Phone conversation between Mr. John Brokaw, USACHPPM, and Dr. Gerry Stelma, USEPA National Exposure Research Laboratory, 10 June 1998, subject: Effective Disinfection of Mycobacteria.

49. Snicer GA, Malley JP, Margolin AB, Hogan SP. Evaluation of ultraviolet technology in drinking water treatment. Original presentation at the Water Quality Technology Conference (WQTC) of the American Water Works Association (AWWA), Boston, MA, November 1996.

50. Phone conversation between Mr. John Brokaw, USACHPPM, and Dr. Barry Fields, Centers for Disease Control and Prevention (CDC), Respiratory Diseases Laboratory, 22 July 1998, subject: Alternative Disinfectants for Mycobacteria.

## ACKNOWLEDGMENTS

We would like to acknowledge all the medical staff of the BMT unit, Hematology-Oncology ward, and the Preventive Medicine Services, Brooke Army Medical Center, for their complete assistance during this investigation. Our appreciation is also extended to Ms. Christina Polyak, Ms. Sandy MacDonald and Ms. Carol Pace, Epidemiology Services Program, USACHPPM, for their administrative assistance and to COL (Dr.) Robert F. DeFraites, Directorate of Epidemiology and Disease Surveillance, USACHPPM, for his expert advice and review of this document.

**TABLES and FIGURES**

Table 1. Demographic, Clinical Features and Type of Mycobacterial Infections in RGM Cases, BAMC, May 1997 – May 1998

| | Age/Sex | Race | Mil Status | Diagnosis | Chronic Conditions | RGM Type | Infection Site | Mo/Yr | Outcome |
|---|---|---|---|---|---|---|---|---|---|
| 1 | 57/F | Caucasian | Dep | Breast Ca | | *M. fortuitum* | Bacteremia | May 97 | Resolved |
| 2 | 49/F | Caucasian | Dep | Non-Hodgkins Lymphoma | Rheumatoid Arthritis | *M. fortuitum* | Bacteremia | Aug 97 | Resolved |
| 3 | 44/F | Caucasian | Dep | Breast Ca | | *M. chelonae* | Bacteremia | Sep 97 | Resolved |
| 4 | 53/F | Caucasian | Dep | Breast Ca | | *M. fortuitum* | CV cath tip | Oct 97 | Resolved |
| 5 | 74/M | Caucasian | Ret Mil | Myelodysplastic Syndrome | Anemia Thrombocytopenia | *M. fortuitum* | Knee effusion | Nov 97 | Resolved |
| 6 | 52/F | Black, non-hisp | Dep | Breast Ca | Hypertension Hypothyroidism | *M. chelonae* | CV cath tip Bacteremia | Nov 97 | Resolved |
| 7 | 27/F | Caucasian | Dep | Breast Ca | | *M. chelonae* | CV cath tip | Jan 98 | Resolved |
| 8 | 55/F | Caucasian | Dep | Breast Ca | | *M. fortuitum* *M. chelonae* | Bacteremia | Mar 98 | Died of Vol. Overload |
| 9 | 58/M | Caucasian | Ret Mil | Breast Ca | COPD | *M. fortuitum* *M. chelonae* | CV cath tip Bacteremia | Mar-Apr 98 | Resolved |
| 10 | 58/F | Caucasian | Dep | Breast Ca | Hypertension Migraine | *M. abscessus* | CV cath tip? Bacteremia | Apr 98 | Resolved |
| 11 | 28/M | Hispanic | AD Mil | Non-Hodgkin's | | *M. fortuitum* | CV cath tip | May 98 | Resolved |
| 12 | 45/F | Caucasian | Ret Mil | Breast Ca | Depression | *M. abscessus* *Actinomyces* | CV cath tunnel? Bacteremia | May 98 | Resolved |
| 13 | 49/F | Caucasian | Dep | Breast Ca | | *M. chelonae* | CV cath tunnel | Apr-Jun 98 | Resolved |
| 14 | 44/F | Caucasian | Dep | Breast Ca | | *M. chelonae* Nocardia spp. | Bacteremia | May-Jun 98 | Resolved |

Table 2. Number and Rate (%) of Bone Marrow Transplants at BMT unit, BAMC, FY93 to FY98 (October 1992 to May 1998)

| Fiscal Year | No. RGM Infections | No. Transplants | RGM Infection Rate (%) |
|---|---|---|---|
| 93 | 0 | 33 | 0.0 |
| 94 | 0 | 36 | 0.0 |
| 95 | 0 | 40 | 0.0 |
| 96 | 0 | 49 | 0.0 |
| 97 | 3 | 90 | 3.3 |
| 98 | 10 | 75 | 13.3 |

**NOTE: Data for FY98 only for period of Oct 97-May 98**

Table 3. Patient-to-Staff Ratios by Month and Ward, January 1997 – May 1998

| Month | Patient:Staff Ratio BMT Unit (Ward 5N) | Patient:Staff Ratio Heme-onc (Ward 6W) |
|---|---|---|
| Jan-97 | 8.2 | 12.5 |
| Feb-97 | 6.1 | 11.1 |
| Mar-97 | 6.5 | 12.7 |
| Apr-97 | 8.8 | 9.8 |
| May-97 | 6.1 | 12.3 |
| Jun-97 | 9.7 | 9.6 |
| Jul-97 | 11.2 | 9.4 |
| Aug-97 | 11.6 | 11.0 |
| Sep-97 | 10.7 | 10.7 |
| Oct-97 | 10.0 | 10.5 |
| Nov-97 | 10.4 | 10.0 |
| Dec-97 | 10.0 | 9.6 |
| Jan-98 | 18.0 | 10.0 |
| Feb-98 | 13.5 | 10.5 |
| Mar-98 | 11.3 | 9.5 |
| Apr-98 | 16.6 | 10.8 |
| May-98 | 11.0 | 9.2 |
| TOTAL | **8.7** | **10.5** |

Table 4. Distribution and Rates (per 1,000 patient-days) of RGM and Staphylococcal Infections by Month and Ward, January 1997 – May 1998

| Month | RGMs-5N | Staphs 5N | Pt-days 5N | RGM Rate 5N | Staph Rate 5N | RGMs 6W | Staphs 6W | Pt-days 6W | RGM Rate 6W | Staph Rate 6W |
|---|---|---|---|---|---|---|---|---|---|---|
| Jan-97 | 0 | 0 | 155 | 0.0 | 0.0 | 0 | 1 | 539 | 0.0 | 1.9 |
| Feb-97 | 0 | 0 | 140 | 0.0 | 0.0 | 0 | 1 | 535 | 0.0 | 1.9 |
| Mar-97 | 0 | 0 | 155 | 0.0 | 0.0 | 0 | 0 | 608 | 0.0 | 0.0 |
| Apr-97 | 0 | 1 | 211 | 0.0 | 4.7 | 0 | 1 | 471 | 0.0 | 2.1 |
| May-97 | 1 | 0 | 147 | 6.8 | 0.0 | 0 | 1 | 527 | 0.0 | 1.9 |
| Jun-97 | 0 | 1 | 222 | 0.0 | 4.5 | 0 | 0 | 411 | 0.0 | 0.0 |
| Jul-97 | 0 | 0 | 292 | 0.0 | 0.0 | 0 | 2 | 403 | 0.0 | 5.0 |
| Aug-97 | 1 | 0 | 291 | 3.4 | 0.0 | 0 | 2 | 471 | 0.0 | 4.2 |
| Sep-97 | 1 | 2 | 268 | 3.7 | 7.5 | 0 | 2 | 471 | 0.0 | 4.2 |
| Oct-97 | 1 | 1 | 229 | 4.4 | 4.4 | 0 | 0 | 474 | 0.0 | 0.0 |
| Nov-97 | 1 | 0 | 197 | 5.1 | 0.0 | 1 | 1 | 462 | 2.2 | 2.2 |
| Dec-97 | 0 | 0 | 220 | 0.0 | 0.0 | 0 | 1 | 434 | 0.0 | 2.3 |
| Jan-98 | 1 | 0 | 359 | 2.8 | 0.0 | 0 | 1 | 459 | 0.0 | 2.2 |
| Feb-98 | 0 | 0 | 297 | 0.0 | 0.0 | 0 | 1 | 504 | 0.0 | 2.0 |
| Mar-98 | 2 | 0 | 248 | 8.1 | 0.0 | 0 | 1 | 437 | 0.0 | 2.3 |
| Apr-98 | 2 | 0 | 331 | 6.0 | 0.0 | 0 | 3 | 507 | 0.0 | 5.9 |
| May-98 | 3 | 0 | 220 | 13.6 | 0.0 | 0 | 1 | 468 | 0.0 | 2.1 |
| Jan 97 to May 98 | 13 | 5 | 3982 | **3.3** | **1.3** | 1 | 19 | 8181 | **0.1** | **2.3** |

NOTES: RGMs=*M. fortuitum and M. chelonae*;
Staphs=*S. aureus and S. epidermidis*;
5N = BMT Unit, 6W = Heme-onc Ward

**Table 5. Demographic, medical, and procedure-related characteristics of case and control patients, BAMC, RGM outbreak investigation, June 1998**

| Variable | BMTU | | Heme-onc | Odds ratio | Odds ratio |
|---|---|---|---|---|---|
| | cases | controls ("internal") | controls ("external") | BMTU cases vs BMTU controls | BMTU cases vs Heme-onc controls |
| | (n=14) | (n=23) | (n=23) | | |
| Age (mean) | 49.0 | 44.1 | 43.7 | na | na |
| Female (%) | 79 | 78 | 26 | 1.0 | 10.4* |
| Caucasian (%) | 86 | 64 | 62 | 3.4 | 3.7 |
| Married (%) | 92 | 100 | 77 | 0.3 | 3.2 |
| History of breast cancer (%) | 71 | 78 | 13 | 0.7 | 16.7* |
| History of smoking (%) | 0 | 15 | 24 | --- | --- |
| History of chronic disease (%) | 50 | 26 | 30 | 1.5 | 1.4 |
| In hospital, # of days (mean) | 17.1 | 13.5 | 19.6 | na | na |
| Severe neutropenia, # of days (mean) | 7.2 | 6.1 | 18.7* | na | na |
| Maximum temperature (°F) (mean) | 102.2* | 100.7 | 102.3* | na | na |
| Mucositis during hospitalization (%) | 71* | 74* | 30 | 0.9 | 5.7* |
| Blood culture (+) during hospitalization (%) | 85* | 31 | 60 | 12.1* | 3.7 |
| Central venous catheter, any type (%) | 93 | 100 | 74 | 0.0 | 4.6 |
| Central venous catheter, triple lumen (%) | 86* | 78 | 57 | 1.7 | 4.6* |
| Central venous catheter, brand "A" (%) | 71* | 74* | 9 | 0.9 | 26.3* |
| Central venous catheter, inflammation (%) | 69* | 44* | 13 | 2.9 | 15.0* |
| Stem cells infused, # bags (mean) | 6.4 | 5.8 | na | na | na |
| Stem cells infused, # frozen bags (mean) | 5.0 | 5.6 | na | na | na |

** indicates differences are nominally statistically significant.*

| Table 6. Multivariate analysis, BAMC RGM outbreak investigation, June 1998, BMTU cases (n=14) versus BMTU/Hematology-oncology ward controls (n=46) | | | | | | |
|---|---|---|---|---|---|---|
| **Variable** | ***AOR** | **95% C** | **P value** | ****AOR** | **95%CI** | **P value** |
| Central venous catheter inflammation | 7.63 | 1.32 – 44.08 | **0.02** | 34.79 | 0.67 - 1808.91 | 0.07 |
| Positive blood culture | 6.38 | 1.06 – 38.39 | **0.04** | 33.79 | 0.41 - 2767.18 | 0.11 |
| Brand "A" catheter | 4.85 | 0.44 – 53.11 | 0.20 | 33.72 | 0.79 - 1431.68 | 0.06 |
| Race (caucasian) | 4.06 | 0.62 – 26.74 | 0.15 | 0.28 | 0.003 - 29.08 | 0.59 |
| Gender (female) | 2.95 | 0.47 – 18.66 | 0.25 | 0.11 | 0.002 - 6.48 | 0.29 |
| Mucositis during hospitalization | 1.62 | 0.35 – 7.42 | 0.54 | 0.33 | 0.002 - 41.00 | 0.65 |
| Age (per year) | 1.05 | 0.98 – 1.13 | 0.13 | 1.10 | 0.94 - 1.29 | 0.23 |
| Neutropenia (per day) | 0.93 | 0.82 – 1.06 | 0.27 | 0.80 | 0.47 - 1.34 | 0.39 |
| NOTE: *AOR = Adjusted odds ratio, adjusting for age, gender, and race<br>**AOR = Adjusted odds ratio, adjusting for age, gender, race, and other variables | | | | | | |

Table 7. Summary of Pertinent Events affecting BAMC Potable Water System

| | |
|---|---|
| April 1996 | BAMC operational. Possible question exists concerning adequacy of flushing/disinfecting BAMC water systems. |
| June 1996 | USACHPPM-South issued recommendations for reducing hardness levels to more appropriate levels. Johnson Controls Inc. begins blending unsoftened water from FSH with softener product water to provide BAMC potable water. |
| July 1996 | Depressurization in BAMC due to nearby 12-inch water main break. Opportunity for pathogens and other contaminants to enter into the BAMC potable water system. |
| February 1998 | 32 water samples (50ml each) from taps/ice machine in BMT Unit (BMTU) found to be negative for RGMs. |
| March 1998 | Sampling size increased to 1Liter, thus, increasing the chance of detection of any existing contamination. 3 water samples (1Liter each) of hot/soft (drinking) water and ice positive for RGMs in low concentrations (*M. chelonae*). |
| April 1998 | Bottled water use (for drinking only) began in BMTU on 9 April. |
| | Two sampling events. Eight of 12 (1Liter) water samples from the BMTU (9 taps, 2 showers, 1 ice) positive for RGMs (7 taps for *M. chelonae* and 1 shower for *M. fortuitum*). Sixteen of 18 (1Liter) samples (sinks and fountain) positive for same RGMs. |
| May 1998 | Preventive Medicine personnel discover that BAMC has had no free available chlorine (FAC) residual in soft water since opening of hospital (i.e. for approximately 25 months). |
| | Johnson Controls Inc. installs chlorination system on BAMC soft water system. Manual hyperchlorination attempt begun 13 May. Intended hyperchlorination goal not met. |
| | Chlorination of BAMC soft water system continued erratically since then. |
| | Twelve (1Liter) samples taken from BMTU, Heme-onc ward (6W) and Interventional Radiology Dept taken on 12 May were positive for RGMs. |
| | After hyperchlorination was performed on 14-15 May, 5 (1Liter) samples collected 15 May from BMTU were positive, but were reduced in numbers (qualitatively). BMTU closed on 18 May; patients moved to Heme-onc ward. More samples taken on 22 May from BMTU (n=5) and Heme-onc ward (n=5), hot and soft water, were all positive for RGMs. Clearly, continued hyperchlorination efforts of BAMC water system are unsuccesful. |
| June 1998 | Formal USACHPPM assistance requested on 4 June. EPICON team arrives on 8 June. |
| | On 5 June 6 (I Liter) samples collected [3 within BAMC, 1 from Fort Sam Houston (FSH) distribution system at entry to BAMC, and at raw and treated water at Well #1]. All positive except raw and treated samples from Well #1. Entry to BAMC sample indicates RGMs are colonizing a part of the biofilm in Fort Sam Houston's water distribution system. |
| | Installation of automated chlorination system begun in early June. |
| | Six (1 Liter) samples collected 10 June (1 hot water sample from BMTU, 1 sample of cold water male bathroom 1st floor, 1 from softener #1 backwash rinse, and 1 from each of 3 softener's effluents). Two water softener (#1) resin samples also collected. All positive for *M. fortuitum* and *M. abscessus*. *M. abscessus* isolate from effluent of water softener #2 subsequently found to be similar to a patient's isolate by PCR RFLP analysis at University of Texas Health Center at Tyler (see Tables 9 & 10). |

Table 8. Summary of RGM Analyses (as of 10 June 1998), BAMC Potable Water System

| Date | No. of Samples and Location | Results | Conclusions |
|---|---|---|---|
| 2/?/98 | 32 combined hot/cold water from sink (taps) and ice from BMTU (50 ml samples) | All negative | |
| 3/?/98 | 2 taps and 1 ice from BMTU (1 Liter samples) | All positive (*M. chelonae*) | Drinking water is one possible source of *Mycobacteria* |
| 4/?/98 | 9 taps, 2 showers, 1 ice from BMTU | 8 positive<br>7 taps (*M. chelonae*)<br>1 tap (*M. fortuitum*) | Confirmation of drinking water as possible source of infection |
| 4/?/98 | 17 BMTU taps & 1 drinking fountain | 16 positive<br>*no speciation* | Continued RGM hospital-wide problem with drinking water |
| 5/12/98 | 12 BMTU taps, 6th floor location (Heme-onc ward), & Radiology samples | All positive | Potable water contamination not localized to BMTU |
| 5/14/98 | **Hyperchlorination of hospital plumbing system begun..** | | |
| 5/15/98 | 5 BMTU taps | All positive, number of RGM species markedly reduced | Hyperchlorination probably has some effect on concentration of RGM organisms |
| 5/22/98 | 5 BMTU and 5 Heme-onc ward combined taps | All positive | Continued presence of *Mycobacteria* in potable water |
| 6/5/98 | 3 various taps within BAMC | All positive | |
| 6/5/98 | FSH treated water entry to BAMC | Positive | Water entering BAMC already contains *Mycobacteria* |
| 6/5/98 | FSH raw water from well #1 and treated water leaving main water treatment plant | All negative | Raw well water not a current or consistent *Mycobacteria* source, may be an FSH potable water system biofilm problem |
| 6/10/98 | BAMC water softener effluent (3), softener #1 backwash rinse water, softener #1 resin (2), BMTU hot water tap and male bathroom water | All positive<br>Softener # 1<50 cfu<br>Softener # 2=20-45 cfu,<br>Softener # 3=30 cfu<br>Backwash=2-10 cfu<br>Resin=9-10 cfu | Without quantification in raw water, cannot determine if *Mycobacteria* concentration increases after passing through softeners<br>Possibility that softeners are colonized (e.g. continuing source) with RGMs |

Table 9. Patient and Water Sampling Isolate Identification, May 1997 – May 1998.

| Patient No. | Hosptial Area | Source and Month | Initial ID BAMC | Final ID UTHCT (by PRA) | PFGE Pattern |
|---|---|---|---|---|---|
| 1 | BMTU | Blood May 1997 | *M. fortuitum* | *M. mucogenicum*/ smooth Gant$^{SS}$, Tet$^{R}$, Ceph$^{S}$ | Same as patient #2 |
| 2 | BMTU | Blood Aug.1997 | *M. fortuitum* | *M. mucogenicum*/ rough Gant$^{S}$, Tet$^{R}$, Ceph$^{S}$ | Same as patient #1 |
| 3 | BMTU | Blood Sep. 1997 | *M. chelonae* | *M. abscessus* smooth/rough | Broken DNA Same as patient #8 |
| 4 | BMTU | Cath tip Oct. 1997 | *M. fortuitum* | *M. fortuitum* Tet$^{S}$ | Unique |
| 5 | Non-BMTU | Synovial fluid (knee) Nov. 1997 | *M. fortuitum* | *M. fortuitum* Tet$^{S}$ | Unique |
| 6 | BMTU | CV cath tip Blood Nov. 1997 | *M. chelonae* | *M. abscessus* | Same as $H_2O$ samples |
| 7 | BMTU | CV cath tip Blood Jan. 1998 | *M. chelonae* | *M. abscessus* | Same as $H_2O$ samples |
| 8 | BMTU | Blood Mar. 1998 | *M. fortuitum* | *M. mucogenicum*/ smooth Gant$^{R}$, Tet$^{R}$, Ceph$^{S}$ | Unique |
| | | Blood Mar. 1998 | *M. chelonae* | *M. abscessus* | Broken DNA Same as patient #3 |
| 9 | BMTU | Blood Mar. 1998 | *M. chelonae* | *M. abscessus* smooth/ rough | Broken DNA Unique |
| | | Blood Apr. 1998 | *M. fortuitum* | *M. fortuitum* third biovar sorb (-) Tet$^{R}$, Clari$^{S}$, rough | Unique |
| 10 | BMTU | CV cath site Tissue Apr. 1998 | *M. abscessus* | *M. abscessus* | Unique |
| 11 | BMTU | Blood May 1998 | *M. fortuitum* | *M. mucogenicum* | Unique |
| 12 | BMTU | Blood/ Tissue May 1998 | *M. abscessus* *Actinomyces* | *M. abscessus* | ND |
| 13 | BMTU | Blood Apr. 1998 | *M. chelonae* | *M. abscessus* smooth | Same as $H_2O$ samples |
| 14 | BMTU | Blood May 1998 | Nocardia spp.* *M. chelonae* NA | NA | NA |
| Control Sample #1 | Non-BMTU | Sputum Feb. 1998 | *M. fortuitum* | *M. peregrinum* Tet$^{R}$, Clari$^{SS}$, Ery$^{S}$ | Unique |
| Control Sample #2 | Non-BMTU | Sputum Mar. 1998 | *M. fortuitum* | *M. mageritense* Tet$^{R}$ | Unique |
| Control Sample #3 | Non-BMTU | Aspirate (rt. neck mass) Mar. 1998 | *M. chelonae* | *M. mucogenicum* Tet$^{S}$, Ceph$^{R}$ | Unique |
| Water Sample #1 | BMTU | Cold water Mar. 1998 | *M. chelonae* | *M. abscessus* | Same as $H_2O$ sample #2 |
| Water Sample #2 | BMTU | Cold water Mar. 1998 | *M. chelonae* | *M. abscessus* | Same as $H_2O$ sample #1 |

* reported at another military hospital (WBAMC)
ND = not done; NA = isolate not available for typing
Gant = Gantrisin (sulfisoxazole)
Tet = Tetracycline
Ceph = Cephalothin
Clari = Clarithromycin
PRA = PCR RFLP analysis
BMTU = Bone Marrow Transplant Unit
PFGE = Pulsed-field gel electrophoresis
BAMC = Brooke Army Medical Center
UTHCT = University of Texas Health Center at Tyler
$^{S}$ = susceptible
$^{R}$ = resistant
$^{SS}$ = very susceptible

Table 10. Water Sampling Results, EPICON team visit, 10 June 1998

| Id # | Source | Initial ID BAMC | PFGE Pattern | ID by PRA (UTHCT) |
|---|---|---|---|---|
| 1246 | BMTU Hot Water - Pt room faucet | *M. fortuitum* | B | |
| 1247-1 | Cold Water - 1st floor male latrine | *M. fortuitum* | B | |
| 1247-2 | Cold Water - 1st floor male latrine | *M. fortuitum* | B | |
| 1248 | Backwash Rinse Softener # 1 | *M. fortuitum* | B | |
| 1267-1 | Water Effluent Softener # 1 | *M. fortuitum* | B | |
| 1267-2 | Water Effluent Softener # 1 | *M. abscessus* | Broken DNA | |
| 1267-4 | Water Effluent Softener # 1 | *M. fortuitum* | B | *M. fortuitum*, third biovar. |
| 1267-5 | Water Effluent Softener # 1 | *M. fortuitum* | B | |
| 1268-1 | Water Effluent Softener # 2 | *M. fortuitum* | B | |
| 1268-2 | Water Effluent Softener # 2 | *M. abscessus* | B | *M. abscessus** |
| 1269-7 | Water Effluent Softener # 3 | *M. fortuitum* | B | |
| 1269-8 | Water Effluent Softener # 3 | *M. abscessus* | Broken DNA | |
| 1271-1 | Resin Water Softener # 1 | *M. fortuitum* | B | |
| 1271-2 | Resin Water Softener # 1 | *M. abscessus* | Broken DNA | |

* *M. abscessus* isolate similar to isolate for patient # 10 in Table 9.

PRA = PCR RFLP analysis
PFGE = Pulsed-field gel electrophoresis
BAMC = Brooke Army Medical Center
UTHCT = University of Texas Health Center at Tyler
BMTU = Bone Marrow Transplant Unit

Table 11. Various Potable Water Disinfectants and their Estimated Costs.

| Disinfectant | Capital Expenditure ($1,000) | | Annual O & M Costs ($1,000) | | Comments |
|---|---|---|---|---|---|
| | Localized Floor Treatment[1] | Whole System Treatment | Localized Floor Treatment | Whole System Treatment | |
| Chlorine | 4.7[2]/floor +$ for contact tank | 0[3] + $ for contact tank | 1.5-1.7[4]/flr | 7.6 - 10.6[4] | Provides residual, however, residuals and contact times used in commonly accepted disinfection practices appear to have very little affect on *Mycobacteria* populations. May not be effective choice to provide long-term protection from *Mycobacteria.* |
| MIOX[5] | 17.0[6]/floor | No info. avail. | 1.9[7] | 5.9[8] | New technology. Residuals similar to chlorine, but much stronger. May have to "play" with required residual to control *Mycobacteria.* Known 4-log reduction of *Bacillus subtilis* spore (more difficult to kill than Giardia, less than Crypto) with 4.0 mg/L with 60-minute contact time. |
| UV[9] | 31.0[10]/ floor | 140.0[10] | 1.8[11] | 8.7[11] | UV won't provide residual. Still will need to provide central rechlorination to make up for FAC stripping at the softeners. |

1. Based on reported design flow of 60 gpm/floor.
2. Complete flow-controlled hypochlorinator system from vendor quote and from reference 33.
3. No additional capital cost since hypochlorinator is already in place.
4. From the equation in reference 40: OM, cents/kgal = 66.0[Avg. Daily Flow, kgal]$^{-1}$ + 0.67[chlorine dose, mg/L] for range of 5-7 mg/L assumed dose. Labor not included (assumed to be a part of Johnson Controls Inc. O&M contract).
5. Mixed Oxidant Technology.
6. Vendor general figure for system to provide 4 mg/L dosage for 60 gpm flow. Price includes $5,000 for 5kgal contact tank to provide 60-minute contact time [(60 gpm X 60 min.) /0.7 short circuiting safety factor].
7. Cost estimated at 1/3 cost of the 0.5 MGD operation from reference 41, including salt and energy costs.
8. Cost for operation only comparable to existing 0.5 MGD plant from reference 41, including salt and energy cost.
9. UV costs from reference 39, in August 1995 dollars.
10. Includes equipment, engineering (10% of equipment), legal, fiscal and administrative costs (3% of equipment) as well as interconnecting piping (6% of equipment) and contingencies (1% of equipment).
11. Includes parts replacement & power. Labor not included (assumed to be part of Johnson Controls Inc. O &M contract).

Table 12. Comparative Resistance of *Mycobacteria spp.* to Chloramines

| ORGANISM | Chloramine Concentration (mg/L) | CONTACT TIME (HOURS) 0 | .5 | 1 | 2 | 4 | 8 | 12 | 24 |
|---|---|---|---|---|---|---|---|---|---|
| | | | Survival (%) | | | | | | |
| *M. avium* 723* | 1.0 | 100 | 99 | 98 | 97 | 96 | 90 | 88 | 85 |
| | 3.0 | 100 | 96 | 96 | 95 | 92 | 85 | 78 | 0 |
| | 6.5 | 100 | 90 | 82 | 0 | 0 | 0 | 0 | 0 |
| *M. avium* 743* | 1.0 | 100 | 98 | 98 | 96 | 96 | 96 | ** | 84 |
| | 3.0 | 100 | 98 | 98 | 97 | 92 | 85 | ** | 0 |
| | 6.5 | 100 | 79 | 55 | 0 | 0 | 0 | 0 | 0 |
| *M. intracellulare** | 1.2 | 100 | 97 | 96 | 93 | 91 | 77 | 58 | 0 |
| | 3.0 | 100 | 97 | 95 | 90 | 95 | 67 | 0 | 0 |
| | 6.5 | 100 | 89 | 80 | 0 | 0 | 0 | 0 | 0 |
| *M. kansasii* | 1.2 | 100 | 98 | 80 | 82 | 73 | 58 | 0 | 0 |
| | 3.0 | 100 | 78 | 65 | 0 | 0 | 0 | 0 | 0 |
| | 6.5 | 100 | 69 | 0 | 0 | 0 | 0 | 0 | 0 |
| *M. gordonae* | 1.6 | 100 | 98 | 89 | 84 | 76 | 54 | 0 | 0 |
| | 3.0 | 100 | 95 | 86 | 81 | 66 | 0 | 0 | 0 |
| | 6.5 | 100 | 72 | 0 | 0 | 0 | 0 | 0 | 0 |
| *M. fortuitum* | 1.5 | 100 | 92 | 85 | 68 | 0 | 0 | 0 | 0 |
| | 3.0 | 100 | 84 | 63 | 0 | 0 | 0 | 0 | 0 |
| | 6.5 | 100 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| *M. chelonae* | 1.6 | 100 | 92 | 89 | 83 | 80 | 76 | 60 | 0 |
| | 3.0 | 100 | 85 | 79 | 71 | 62 | 54 | 0 | 0 |
| | 6.5 | 100 | 43 | 0 | 0 | 0 | 0 | 0 | 0 |

NOTE: Extracted from reference 36.
*Species that make up the *M. avium* complex.
** Contaminated samples removed from study.

Figure 1. Hot Water Distribution System, Brooke Army Medical Center, 15 Risers

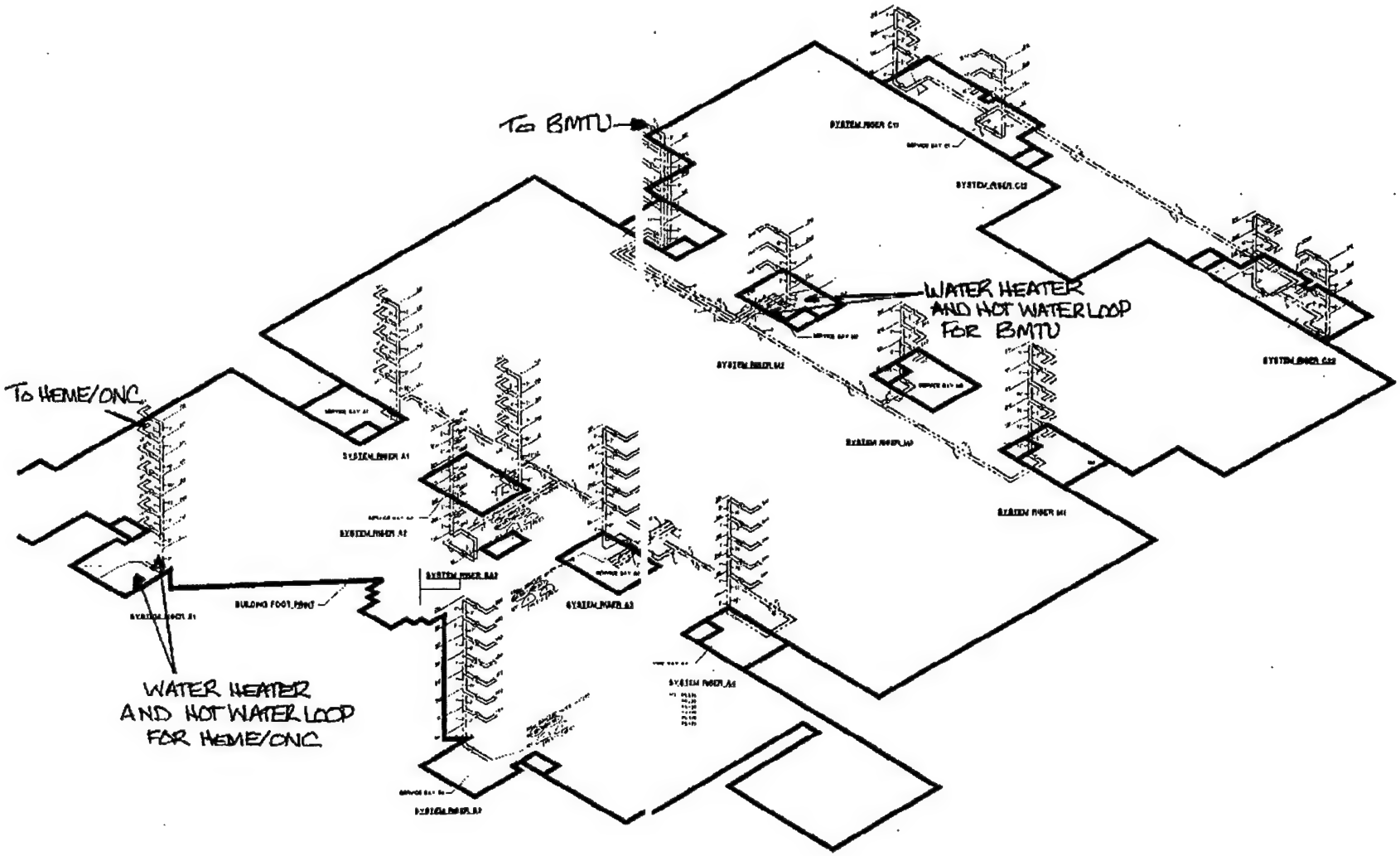

To BMTU
WATER HEATER
AND HOT WATER LOOP
FOR BMTU
To HEME/ONC
WATER HEATER
AND HOT WATER LOOP
FOR HEME/ONC

Figure 2. Softened Water Distribution System, Brooke Army Medical Center, 15 Risers

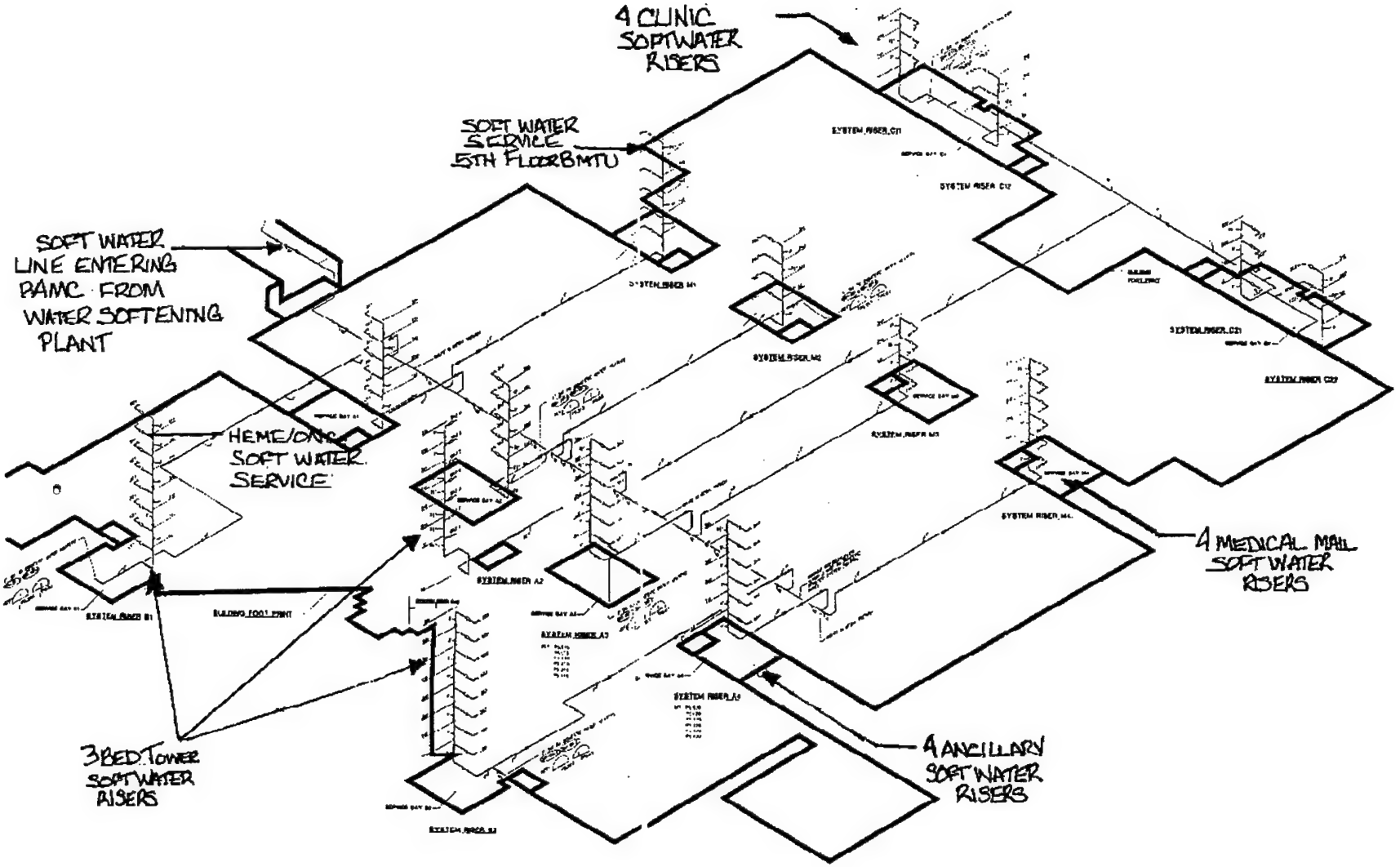

4 CLINIC SOFTWATER RISERS
SOFT WATER SERVICE 5TH FLOOR BMTU
SOFT WATER LINE ENTERING RAMC FROM WATER SOFTENING PLANT
HEME/ONC SOFT WATER SERVICE
4 MEDICAL MAIL SOFT WATER RISERS
3 BED TOWER SOFT WATER RISERS
4 ANCILLARY SOFT WATER RISERS

Figure 3. Illustration of Water Softeners at Brooke Army Medical Center

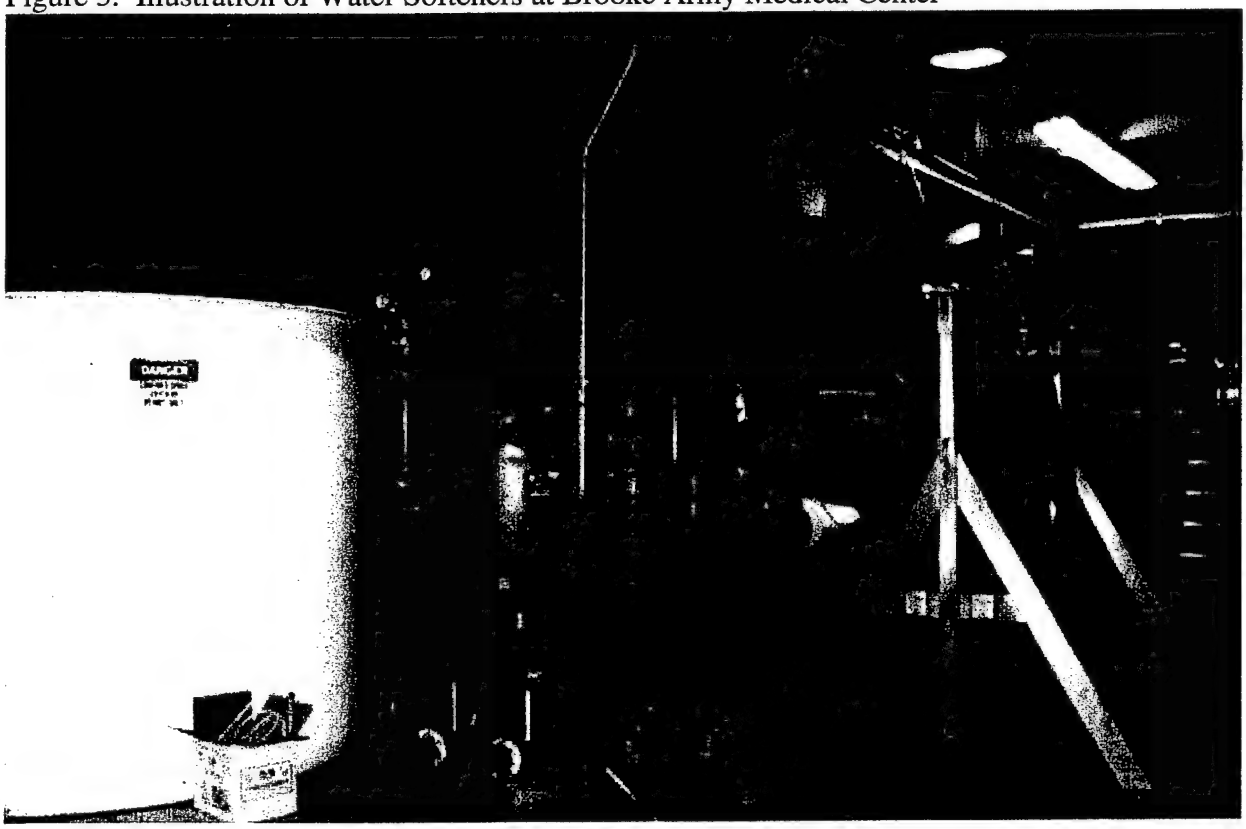



Figure 4. Illustration of Automatic Metering Valve (blue device)

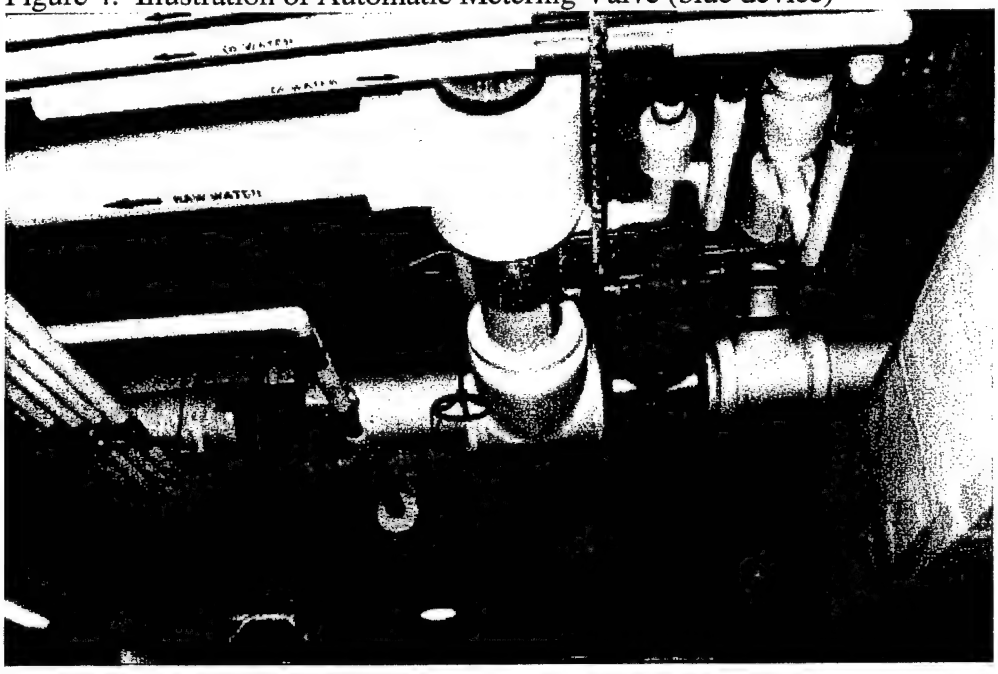


**Figure 5. Infection rates among hospitalized patients, bone marrow transplant (BMT) and hematology-oncology units, Brooke Army Medical Center, January 97 - May 98**

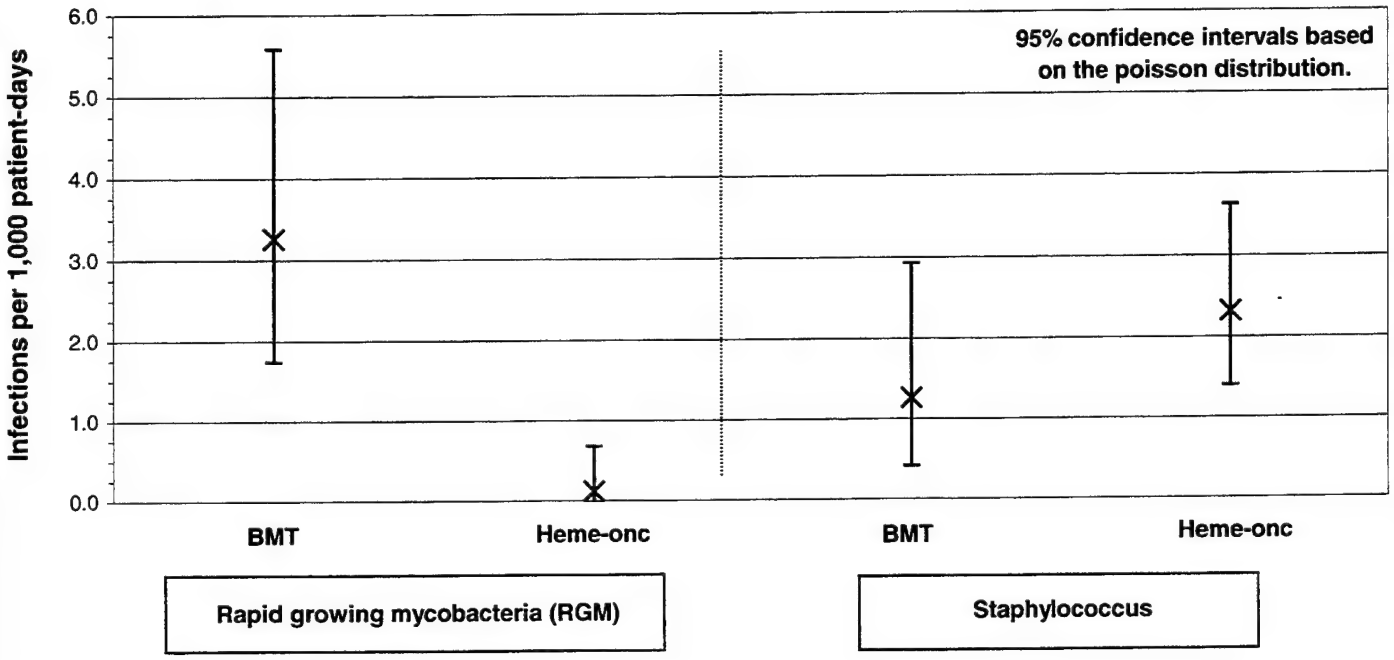


**Figure 6. Distribution of central venous catheter placements among RGM cases and non-cases, by radiologist who performed insertion procedure, Brooke Army Medical Center, January 1997 - May 1998**

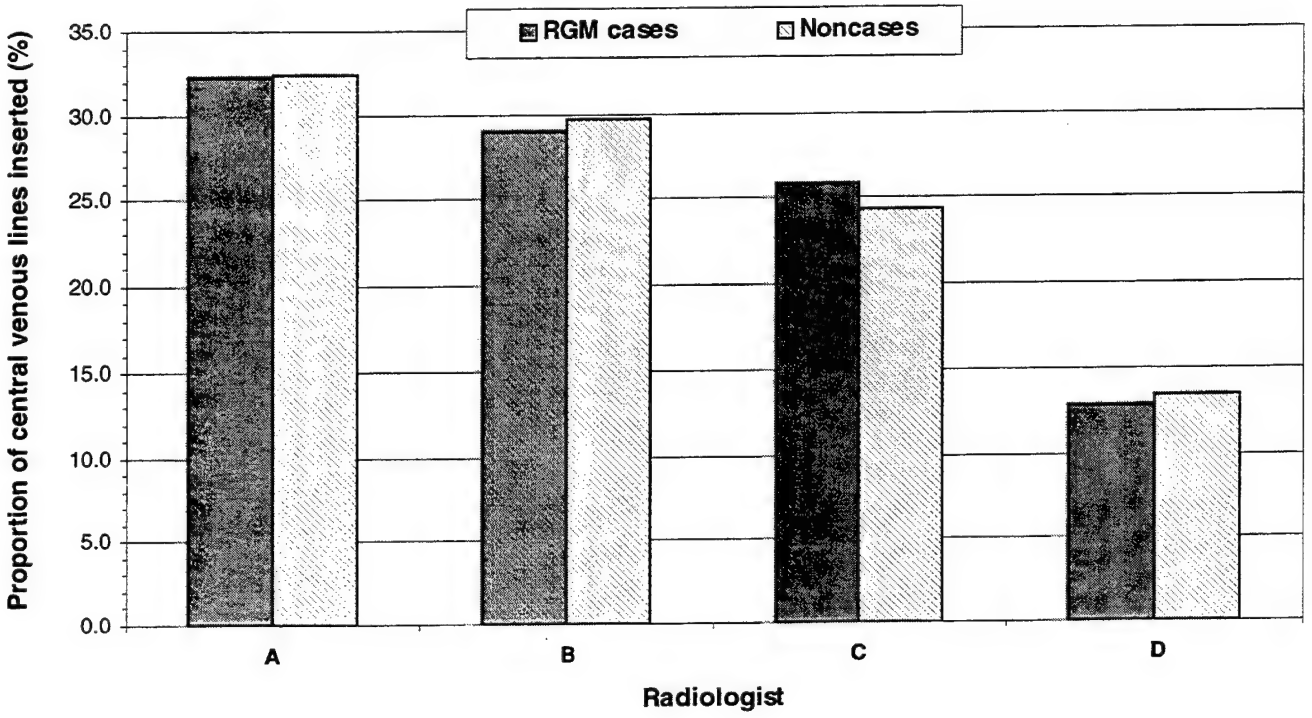
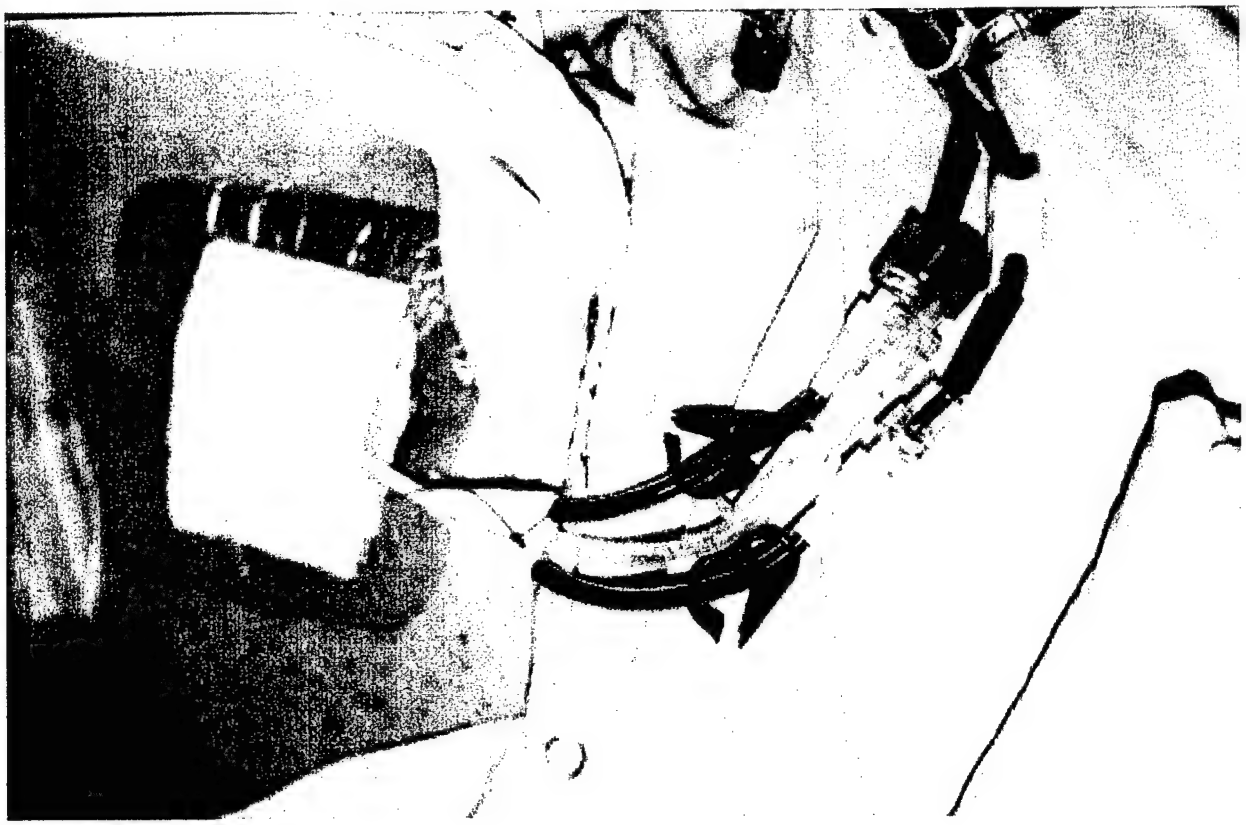


Figure 7. Triple-lumen central venous (CV) catheter, Company A brand.



# Appendix A

MCHE-MDI 7 June 98

MEMORANDUM

FROM: MAJ Robert M. Plemmons, Chairman, BAMC Infection Control Committee

TO: EPICON team from CHPPM

SUBJECT: summary of events surrounding the outbreak of infections due to rapidly growing mycobacteria in bone marrow transplant patients at BAMC

1. Since May 1997, we have identified 13 total patients who underwent bone marrow transplant (BMT) at BAMC and subsequently developed bacteremia and/or central line site infection with rapidly growing mycobacteria (RGM), specifically with *Mycobacterium fortuitum* and *Mycobacterium chelonae*. An additional BAMC Oncology patient who was not a BMT patient developed septic arthritis due to *M. fortuitum* during this period. Per Oncology, roughly 100 patients have had BMTs at BAMC since May 1997. The background incidence of RGM bacteremia at BAMC prior to this outbreak had been zero. One of the BMT patients with the RGM bacteremia died and she had a positive blood culture less than one week prior to her death, but her death was officially attributed to metastatic breast cancer (confirmed at autopsy). Some of the other infected patients experienced significant morbidity and required parenteral antibiotic therapy and, in at least one case, surgery to cure their infections, but there have been no other deaths among these patients.

2. What follows is a chronological account of the outbreak and the activities surrounding it:

MAY 97 - **first** case of RGM bacteremia (*M. fortuitum*) identified in a BMT patient

AUGUST 97 - **second** case of RGM bacteremia (*M. fortuitum*) identified in a BMT patient

SEPTEMBER 97 - **third** case of RGM bacteremia (*M. chelonae]* identified in a BMT patient

OCTOBER 97 - cluster of cases recognized; all three patients had developed fever within three days of stem cell infusion; a formal evaluation of bone marrow stem cell storage, processing, and infusion was undertaken by Infection Control; no recent changes in BMT procedures were noted and no problem areas were recognized at that time, but use of tap water to warm the bags of stem cells prior to infusion was noted; **fourth** case of RGM infection identified in a BMT patient (central catheter tip culture grew *M. fortuitum*)

NOVEMBER 97 - **fifth** case of RGM infection identified (septic arthritis due to *M. fortuitum* in a non-BMT Oncology patient); **sixth** RGM infection identified (*M. chelonae* bacteremia in a BMT patient); a review of Interventional Radiology procedures was undertaken since BMT patients had central lines placed pretransplant; BMT nursing protocols for line care and flushing were reviewed; additional review of stem cell handling; again, no potential sources of contamination recognized

JANUARY 98 - **seventh** case of RGM infection identified (*M. chelonae* bacteremia in a BMT patient)

FEBRUARY 98 - cultures performed on 32 small volume (50cc) water specimens from sinks and ice machine in BMT unit; no RGM were recovered form any of these water specimens

MARCH 98 - **eighth** case identified (mixed bacteremia with *M. fortuitum* and *M. chelonae* in a BMT patient; a blood culture drawn one week later from same patient grows *M. chelonae* alone); 3 specimens (roughly one liter each) of hot and cold water from the BMT unit kitchen sink and ice from the unit ice machine and 16 specimens of soap from unit soap dispensers are submitted for AFB culture; **ninth** case identified (*M. chelonae*) bacteremia in a BMT patient; this patient would have a second positive blood culture in April, this time for *M. fortuitum*); all three specimens of water/ice submitted earlier grow RGM (*M. chelonae*), soap cultures all negative

APRIL 98 - BMT unit switches to bottled water for drinking (all other uses of tap water continue as before); catheter sites for BMT patients are covered with op-site and taped prior to showering; outbreak discussed with Dr. Barbara Brown if UTHC-Tyler (RGM authority); 12 one liter specimens of water from BMT unit (9 sinks, 2 showers, ice machine) submitted for AFB culture - 7 sinks positive for *M. chelonae*, 1 sink for positive for *M. fortuitum*, both showers and ice machine negative for RGM; outbreak reported at BAMC Quality Improvement Committee meeting; **tenth** case identified (*M. chelonae* bacteremia in BMT patient, culture drawn prior to bottled water use); 18 one liter samples (more BMT unit sinks and water fountain) submitted for AFB culture, 16/18 positive for RGM (all water cultures to-date have also shown heavy growth of non-RGM bacteria)

MAY 98 - representative RGM isolates from patients and water sent to UTHC-Tyler for molecular strain typing; meeting between Infection Control representatives and Mr. Roy Hirchak of Facilities Management Branch (63241/64534) to discuss RGM in water; finding that BAMC water contains too little chlorine due to removal by water softener; proposal made to install chlorinator downstream from water softener; **eleventh** case identified (*M. fortuitum*) bacteremia in a BMT patient; culture drawn after switch to bottled water); meeting of Infection Control representatives with acting DCCS, Chief of Medicine, Chief of Oncology Service, Director of BMT unit, and LTC Tannen to discuss options for dealing with outbreak given latest case; decision made to have current BMT patients bathe in bottled water and to put planned BMTs on

hold pending hyperchlorination of the water; hyperchlorination to roughly 4-6 ppm took place for 24 hours on 14-15 May; chlorinator installed; cultures of water that had been collected from the BMT Unit, Ward 6-West (Oncology), and Interventional Radiology just prior to hyperchlorination all grew RGM; cultures of water collected from BMT unit the day after hyperchlorination also grew RGM but in reduced numbers (numbers of non-RGM species were markedly reduced); outbreak reported at BAMC Infection Control Committee meeting; BMT unit closed, but BMTs resume with the patient's being cared for on Ward 6-West with continued avoidance of tap water (nurses must wear gloves when handling catheter); decision made to ask for assistance from CHPPM; **twelfth** case identified (BMT patient with RGM bacteremia and line site infection; in BMTU prior to water avoidance practices)

JUNE 98 - **thirteenth** case identified (BMT patient with RGM line site infection, in BMTU prior to total tap water avoidance measures); there may still be another case, but this has not yet been confirmed; after review of stem cell infusion procedure. BMTU notified to stop warming stem cell bag in tap water prior to infusion; test for water contamination during immersion of stem cell bad in dyed water shows contamination of infusion port with water during removal of protective cap; BMTU staff made aware of above finding; CHPPM arrives

3. Potential links between contaminated tap water and bloodstream infections include:

   A. bathing in heavily contaminated water with lone site inadequately protected
   B. contamination of stem cell bags during warming in tap water bath with subsequent contamination of catheter hub during handling
   C. transfer on hands of nurses after washing hands in contaminated water
   D. ingestion of contaminated water with subsequent bloodstream invasion in the setting of mucositis
   E. multi-use medication vial contaminated with tap water

4. Information that supports/refutes above theories (no single explanation fits all cases):

   A. small number of BMT patients on unit at any one time meant that water use was minimal and opportunity for stagnation and microbial proliferation increased; virtually all of the patients bathed on the unit; lack of recovery of RGM from cultures of shower water may have reflected recent use and flushing to less than detectable numbers; 6-West (Oncology) had more and sicker patients, more shower use, and essentially no RGM infections.
   B. per Mr. J. Myhand (BMTU Director), not all of the infected BMT patients received cells that were warmed in tap water; at least one became infected prior to stem cell infusion.
   C. not all of the infected patients had mucositis; patients on Ward 6-West with worse mucositis and more profound immunosuppression have not become infected; the one patient who was not on the BMTU (fifth case, septic arthritis) had myelodysplastic syndrome and came into the hospital for transfusions reportedly, no multi-use vials in use at any time during outbreak.

5. Additional issues:

   A. ongoing mycobacterial contamination of hospital water; best way to clean it up?
   B. change to new type of triple-lumen catheter (Neostar) just prior to outbreak; increased risk for infection with larger catheter?
   C. problem (in terms of water quality) with location of BMTU in hospital; is there a better location? Augmented water purification system for BMTU?

6. Please feel free to contact me at any time with questions pertaining to the above issues.

Robert M. Plemmons
MAJ, MC, USAR
Chairman, Infection Control Committee
Brooke Army Medical Center

Phone: (W) DSN 429-2446
Fax (210) 916-0388
E-mail: MAJ Robert Plemmons at
MEDCEN12_BAMC

# Appendix B

Hyperchlorination Procedures

1. Using localized chlorination system or central water treatment plant sodium hypochlorite injection system increase disinfectant feed rate such that > 5ppm free available chlorine (FAC) is entering subject location (BMTU or Hematology-Oncology Ward or other specific riser undergoing chlorination). A 10ppm residual entering the area is a good place to start. This allows for dissipation of residual over distance and time.

2. Open first water fixture within the subject ward closest to the point of disinfectant application. Flush until >5ppm FAC is detected.

3. Open next water fixture along the plumbing system. Flush until >5ppm FAC is detected. Open and flush all fixtures in subject ward in an identical manner.

4. Once a >5ppm FAC has been detected in at all fixtures scheduled for hyperchlorination, begin timing the 24 hour contact time. All plumbing must be in contact with at least >5ppm for 24 hours.

5. Set sodium hypochlorite feed rate so that it will provide at least 5ppm FAC to any new water entering the plumbing system.

6. Control water use by limiting use to one tap/toilet so that flow entering water system does not exceed capacity of disinfection system to provide >5ppm FAC.

7. If step #6 is not possible, an automatic disinfection system capable of increasing feed rates with increasing flow will be necessary.

8. At the end of the 24hr contact time, test FAC residuals at random locations through-out subject ward to ensure that 5ppm FAC. If residual is not $\geq$5ppm, process must be repeated. More frequent residual sampling to detect decreases in FAC may be more appropriate so that disinfectant feed rates can be adjusted prior to slipping below 5ppm FAC.